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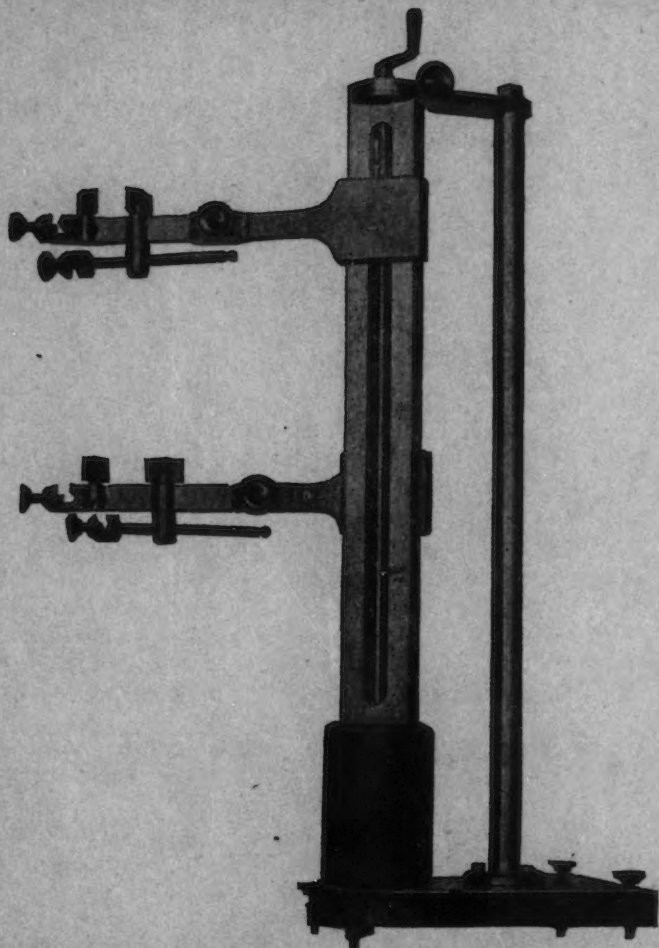
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THE AMERICAN JOURNAL OF PHYSIOLOGY

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THE PROGRESS OF PHYSIOLOGY

AUGUST KROGH

I suppose that almost every worker in our science has given some thought to the general progress of physiology and to the problems raised by its growth, and I cannot doubt that some have pondered deeply over these problems and have much more insight into them than I possess, but you must admit that on the whole the thoughts have been kept private, and nobody seems to have considered it worth while to bring the matter up for a general discussion among physiologists. When I venture to do so it is because I feel deeply the importance of the subject, and in spite of the fact that I feel even more deeply my own lack of competence in all questions involving organization. My aim is only to draw your attention to some of the problems in the hope that means may be found to solve them.

We are all aware that physiology is a rapidly expanding science in the sense that an ever increasing amount of work is being produced by an increasing number of workers, and the increase in attendance at the international congresses bears witness to the fact. I have tried to count from the abstracting and indexing journals the number of papers published on physiological subjects. The figures are probably not strictly comparable, but their general tendency is unmistakable. In the first year of this century, the year of the Congress in Turin, titles were given in the *Physiologisches Zentralblatt* of 3800 papers, and during the first decade only minor fluctuations took place. I find from the *Zentralblatt* and *Bibliographia* 3900 in 1904 (Congress in Brussels), 3500 in 1907 (Heidelberg) and 4300 in 1910 (Vienna), but then a rapid increase took place and in 1912 the figure was 6700. I have no reliable statistics for the years from 1913-1919, but for 1920 the *Jahresbericht* gives the titles of 11,500 papers; for 1923 (Edinburgh) the figure is 14,000 and for 1926 (Stockholm) it reached 18,000, and there is no doubt that it is increasing further. I had the impression that physiological papers now were on an average shorter than 25 years ago, but a sample counting failed to substantiate this im-

pression and showed the average length to be then as now 10 pages. The increase in publication is due to a number of causes and to some extent it may be unreal and due to more complete indexing now, but there can be no doubt that much more work is done now and by a larger number of workers than 25 years ago. It is interesting to note that according to the *Zentralblatt* for 1901 only 100 papers or 2½ per cent were published in America or by American authors while the *Berichte* for 1926 shows about 3500 American papers, nearly 20 per cent of the total.

Our science has grown also in the sense that our understanding of many problems of fundamental importance has been broadened and deepened. We are all more or less familiar with the enormous expansion of knowledge in the field of nutrition and in the study of hormones. Less spectacular, but, I think, equally important progress has been made in the physiology of muscle and nerve and in the problems of the circulation. We have become acquainted recently with the long continued work of Pavlov and his school on the cerebral functions, and I think we can say that the investigation of the nervous system is making satisfactory progress in spite of its tremendous complication.

Physiology has been brought in much closer contact with the allied and fundamental sciences. Twenty years ago the application of statistical and mathematical analysis to our problems was very uncommon and unfamiliar to most physiologists, and there were even those who deprecated it violently. Though there is still room for much further progress the statistical weapons are wielded successfully by a large and increasing number of investigators.

In many ways the results and methods of pure chemistry and physics are utilized and successfully-adapted to our problems, and I trust we can claim some reciprocity, since the use of micromethods, initiated mainly within our domain, where their services are invaluable, is spreading to other provinces of science. It is extremely gratifying from a general point of view to see how even the most advanced ideas and methods of physics and chemistry are inspiring the work of a few of our colleagues. I use the words "from a general point of view" on purpose, because for my own part the fact shows me that development is taking place along lines where I cannot follow and I believe we have to admit that with the rate at which advance is now taking place in the sciences the useful span of life in the front line of research is likely to be cut short for many of us, because our viewpoints and even our methods become antiquated.

While we have every reason to rejoice over the growth and progress of our science I think we must admit at the same time that there is room for much improvement and even that some aspects of the situation are unsatisfactory. Physiology is growing unwieldy. It is impossible for any single human being to be familiar with modern physiology in all its branches

in the sense in which the great teachers of 20 or more years ago were familiar with the physiology of their time. We have to face the splitting up of physiology into more or less separate and independent sciences, and we are confronted with the problem of finding the right lines of cleavage. Research is bound up closely with teaching, and the lines of cleavage are determined and will be determined to a very large extent by the university chairs and departments which are brought into existence. It is the practical teaching situation which has made pharmacology an independent science, while as a branch of research it can scarcely be distinguished from pure physiology. We have seen biochemistry grow up and obtain independent chairs and laboratories in the universities of many countries, and I believe we all agree that this has been a most happy development which will be carried on into those universities and medical schools which have not yet effected the separation.

A few universities, and Copenhagen among them, have made a new departure in creating separate chairs and department for biophysies. This is justified from the point of view of teaching and for other practical reasons, but I do not think it is the thing most urgently needed from the point of view of research with which we are here concerned. Our physical problems have so far usually been rather elementary, but I must admit that the situation is rapidly changing and it is quite possible that new discoveries like that of radiations from rapidly growing tissues may in a near future make biophysical departments generally desirable or even necessary.

It is natural and useful that laboratories specialize in certain directions, and such specialization is sometimes accentuated by their official status, so that they may be laboratories for the study of definite problems or groups of problems as endocrinology, muscular work, etc. I do not think however that cleavage of physiology along such lines will become permanent or general, and I feel sure that harmful results would be inevitable if it did become general and effective. The activities of the organisms which we are studying are too intimately correlated to allow much specialization of this kind. A serious attack on any definite problem may lead into a different province of physiology, and fortunately the workers are usually free to carry on the attack regardless of artificial boundaries.

Physiology as a science has taken its origin from the necessities of practical medicine, and even now the large majority of workers in physiology have had the benefit of a medical education and hold their appointments in medical schools. Nevertheless we all hold physiology to be an independent science, and most of the work done in physiological laboratories has no direct relation to medicine. The line of development which I think should be followed is to establish in one direction a branch of physiology which is much more intimately in contact with practical

medicine and in the other direction a branch which is much more independent.

I think that work done on this side of the Atlantic has contributed more than anything else to the growing understanding of the fact that the problems of disease are mainly physiological and cannot be solved by the methods of clinical observation, morbid anatomy, bacteriology or serology alone, even in cases where these sciences are absolutely essential. It is the functional reaction of the organism to the attack of disease and to the therapeutic measures which is after all the central problem. A large and increasing proportion of physiological research is carried on in hospital laboratories by men and women who are at the same time practising the art of healing. Much of this work is very valuable, but sometimes the outlook is rather narrow, and I believe that a great deal could be gained by expert physiological direction and coördination. I think the time has come when special chairs and laboratories should be established for the physiology of disease, morbid physiology or experimental medicine, if you prefer that name. The main point is that the leaders of such laboratories should have no regular duties connected with the treatment of patients, but they must have a small number of beds at their disposal for the temporary study of selected cases, and they must of course be in close and constant contact with the clinical wards. It goes without saying that they must have facilities for studying disease experimentally on animals. Within the field of blood circulation and innervation of blood vessels with which I am personally acquainted, I have had the desirability and even necessity of coöperation with the practical medicine brought home to me again and again. I have learned also that the theoretical problems regarding kidney function require for their solution a close study of clinical cases, and I cannot doubt for a moment that great benefit to patients will ultimately result from such a study. Much can be done in this direction by means of existing facilities, but I anticipate an acceleration of progress from the creation of special chairs as outlined, and I feel sure that the resulting contributions to practical medicine would amply and within a short space of time repay the communities for the initial outlay on such departments and for their maintenance.

The other line of development which I would suggest is not perhaps such a pressing need, but ultimately I believe it to be of scarcely less importance. It is the creation in the science schools and in close coöperation with the departments of zoölogy of chairs and laboratories for comparative physiology, animal physiology or zoöphysiology. The name does not matter much, though I confess that there is one name with which I have no sympathy,—that of "general" physiology. I suspect that it is often used to denote just those aspects of a problem which are considered most important from an individual point of view. In my opinion a general

physiology which can describe the essential characteristics of matter in the living state is an ideal to which we may hope that our successors may attain after many generations, and I want to emphasize that the route by which we can strive toward the ideal is by a study of the vital functions in all their aspects throughout the myriads of organisms. We may find out, nay, we will find out before very long the essential mechanisms of mammalian kidney function, but the general problem of excretion can be solved only when excretory organs are studied wherever we find them and in all their essential modifications. Such studies will be sure, moreover, to expand and deepen our insight into the problems of the human kidney and will prove of value also from the narrowest utilitarian point of view.

For a large number of problems there will be some animal of choice or a few such animals on which it can be most conveniently studied. Many years ago when my teacher, Christian Bohr, was interested in the respiratory mechanism of the lung and devised the method of studying the exchange through each lung separately, he found that a certain kind of tortoise possessed a trachea dividing into the main bronchi high up in the neck, and we used to say as a laboratory joke that this animal had been created expressly for the purposes of respiration physiology. I have no doubt that there is quite a number of animals which are similarly "created" for special physiological purposes, but I am afraid that most of them are unknown to the men for whom they were "created," and we must apply to the zoologists to find them and lay our hands on them.

I want to say a word for the study of comparative physiology also for its own sake. You will find in the lower animals mechanisms and adaptations of exquisite beauty and the most surprising character, and I think nothing can be more fascinating than the senses and instincts of insects as revealed by the modern investigations.

Just as in the case of pathological physiology, a good beginning has been made in the study of this group of problems and an increasing number of papers are published which can be justly classed as comparative or zoophysiological. There are a few chairs and departments in this branch of our science, but I suggest that it is time to increase their number, to coördinate efforts, to offer and to invite coöperation with zoology departments, with field biology and zoological investigation also along the morphological lines. I venture to believe that such coöperation will be fruitful not only to the physiologists seeking it, but also to our elder brethren in the departments of zoology.

The establishment of new chairs and departments requires the sympathetic interest and active coöperation of faculties and university authorities, but there are many points on which we ourselves individually and by our united efforts can improve unsatisfactory conditions in physiology and increase the efficiency of physiological publication.

When I try to picture the evolution of physiological truth I am struck by the similarity with the evolution of life itself upon our planet. Ideas are conceived, facts are elaborated with immense joy and with infinite labour. A large number die without ever coming to the light of publication, and of those which are published an appalling proportion sink to the bottom and can only be dug out as fossils from dusty library shelves. Many succumb in controversies with other ideas and facts and a minority only survive in the sense that they beget new ideas and give rise to the discovery of new facts. I believe that this enormous waste is on the whole inevitable and bound up inseparably with the difficulties which physiological investigation has to overcome. I look upon controversy especially as one of the chief ways in which truth is approached. We may fondly imagine that we are impartial seekers after truth, but with a few exceptions, to which I know that I do not belong, we are influenced and sometimes strongly by our personal bias and we give our best thoughts to those ideas which we have to defend. Nevertheless we should of course all do our best to avoid controversy, in the sense that we should take every possible care to verify our facts and substantiate our conclusions before publishing our results.

When I attempt to pass in review the physiological literature of today I notice certain defects which are too common and which could no doubt be remedied to a certain extent. In a recent small book of instructions for medical writers I find the statement that what is needed in scientific papers is facts and again facts and still more facts. I venture to disagree emphatically with this statement. Facts are necessary, of course, but unless fertilized by ideas, correlated with other facts, illuminated by thought, I consider them as material only for science. I am prepared to submit the thesis, revolting though it may seem, that too many experiments and observations are being made and published and too little thought is bestowed upon them. It is a statement not too infrequently met with in physiological papers that a certain experiment has been repeated on, say, 47 animals. Very often, though by no means always, such a routine procedure is sheer waste of time and animals, and at the root of the apparent diligence lies a mental inertia which carries the experimenter along the accustomed groove with a minimum of exertion of the mind. But physiological experimentation which shall lead to reliable results and carry us forward requires constant exertion, constant attention to details which may be trivial or may turn out to be of vital importance.

When experimental results are found to be in conflict with those of an earlier investigator the matter is often taken too easily and disposed of for instance by pointing out a possible source of error in the experiments of the predecessor, but without inquiring whether the error, if present, would be quantitatively sufficient to explain the discrepancy. I think that dis-

agreement with former results should never be taken easily, but every effort should be made to find the true explanation. This can be done in many more cases than it is actually done; and as a rule it can be done more easily than by anybody else by the man "on the spot" who is already familiar with essential details, but it may require a great deal of imagination and very often it will require supplementary experiments.

It is an almost invariable custom of editors of journals to reject papers which do not contain new "facts." It is natural to be sceptical toward reasoning not supported by facts, but it must happen in many cases and to many physiologists that their thoughts are illumined by facts which were incompletely understood by those who brought them forward, and I remember more than one occasion where published experiments could be given a much more consistent explanation than that adopted by their authors. In such cases a more liberal interpretation of the rules of the journals would serve the interest of our science, and I venture to think that the publication of papers discussing facts already known should be encouraged.

I have said enough and perhaps too much on the things we can do individually. What can we do as a body? The catchword of our post-war times is organization. Can physiology be organized? When I was very much younger I had visions of leaders of physiology who could see clearly the problems to be studied and the ways of approaching them, and who might distribute them and their separate parts among the laboratories and the individual workers. At a somewhat later stage I imagined a central laboratory to which all new methods could be submitted for testing and from which only the most reliable and quickest methods would emanate. I see clearly now that all such schemes are dreams. They can never be realized and should never be realized if it could be done. The individual freedom is our chief asset, the mainspring of the really new ideas, the guarantee of progress. Physiology does not go forward as an ordered line of battle on a continuous front, but must be carried on, as someone has aptly said, as a guerilla warfare against the unknown, conducted singlehanded or by quite small units. There is no need for an extensive organization of research, but there is much need for voluntary coöperation on a limited scale between individuals and laboratories. There are many problems which can only be successfully attacked when experimental physiologists coöperate with histologists, with chemists or physicists or with clinicians, and some problems will require the combined efforts of several of these groups, but the affair is always one of local and voluntary coöperation and does not concern us here.

While I have no faith in organization on a large scale of research I think there is a wide and fruitful field for organization of what we might term the services behind the front. We all feel the difficulties of keeping abreast

of the literature, and I cannot doubt that the methods of indexing, abstracting and reviewing that literature could be improved and organized so as to give better service at less cost. It may be desirable to adopt a system of indexing papers according to the subjects dealt with and, if it is desirable, *one* system ought to be agreed upon and used by all the leading physiological journals and by department libraries throughout the world. It is quite conceivable that even an inferior system universally adopted would be much better than many excellent systems in use locally or a general lack of system.

We have I think a very good abstracting service. I am best acquainted personally with the German abstracts in "Berichte," and a high tribute should be paid to their general excellence and completeness. Very few papers in the leading languages escape their vigilance, but when I look over the numbers one by one as they come to hand to keep myself informed about the subjects in which I am interested I always feel that the distribution and arrangement could be considerably improved.

It is, I think, a wasteful procedure that the same papers are independently recorded and abstracted in several different languages and an even greater number of different abstracting journals. It ought to be possible to obtain some arrangement for exchange of abstracts and other mutual help and thereby effect also a saving in cost. Then there is the difficult question of getting abstracts of papers in less known languages like the Scandinavian or Russian.

I cannot but feel that a large number of separate copies go to waste, because they are distributed to people who cannot utilize them, and that on the other hand separate copies of certain papers may be badly wanted by people who cannot get them. I have been considering for years the possibility of an organization which could prevent some of this waste, but I have to confess that so far I have been unable to discover any workable scheme.

After all, it is not my business to point out to you specific remedies for this or that, but to suggest if possible broad measures which may lead to the solution of some of our difficulties. I believe that the machinery for dealing with problems affecting us all can be created without serious difficulty. The International Congress of Physiology is without any doubt the highest authority in matters pertaining to the organization of physiology and its necessary services. Why should not the Congress exercise this authority?

We have met together for friendly intercourse, to be taught and to teach by demonstration of experiments and discussion of papers. The benefit to our science from a meeting like this is very great, although very difficult to estimate by visible results. Why should we not make this, our Congress, which meets together regularly, into an instrument also for the

organization of our necessary services, for the elaboration of rules of nomenclature and for the protection of our scientific freedom. I believe that it can be done and ought to be done.

Perhaps I am still a dreamer of dreams. I know for certain that I have not that administrative capacity which is necessary to transform my dreams into living realities, but if they contain any idea of any value I venture to hope that our administrators will take up that idea and carry it out to the benefit of our science and the greater glory of our Congress.

SOUVENIRS DES PREMIERS CONGRÈS DE PHYSIOLOGIE

LÉON FREDERICQ

Professeur émérité à l'Université de Liège et président du second Congrès International de Physiologie à Liège, 1892

L'idée première de réunir les physiologistes de tous pays dans des Congrès périodiques est née d'échanges de vue entre Hugo Kronecker et les physiologistes anglais qui avaient travaillé avec lui au laboratoire de Ludwig à Leipzig. C'est à l'instigation de Kronecker, que la *Physiological Society de Londres* adressait à la date du 19 Mars 1888, à 109 Professeurs de Physiologie, une *lettre circulaire*, les invitant à examiner l'utilité qu'il y aurait à se réunir en Congrès l'année suivante et proposant de choisir à cet effet la ville de Berne.

À la suite de cette démarche qui recueillit l'adhésion unanime, un certain nombre de physiologistes anglais, français, allemands, italiens et suisses se réunirent le 10 septembre 1888, à Berne, chez Kronecker et élaborèrent un programme de travaux.

Il fut décidé que les séances du Congrès n'étaient pas destinées à faire la concurrence aux Revues de Physiologie, pour la publication des faits nouveaux. On insista vivement sur ce point que les communications auraient un caractère de démonstration et seraient avant tout consacrées à l'expérimentation. Pour décourager ceux qui auraient été tentés d'y venir lire leur prose, on décida de ne pas imprimer le texte des communications et de ne pas admettre officiellement de représentants de la presse. C'était là quelque chose de tout à fait nouveau dans un congrès international. On décida aussi, sur la proposition de Michael Foster, que la plus grande simplicité présiderait aux réunions générales et qu'on éviterait les fêtes, réceptions et discours officiels.

Comme les locaux du *Hallerianum* de Berne n'étaient pas prêts à ce moment, on décida de se réunir à Bâle, où le nouvel Institut d'Anatomie et de Physiologie, le *Vesalianum*, et celui de Physique et de Chimie (*Bernoullianum*) répondaient à toutes les exigences des expérimentateurs.

Le Professeur Holmgren d'Upsal fut désigné comme Président du Congrès.

Le premier Congrès de Physiologie se réunit à Bâle, l'année suivante, du 9 au 12 Septembre, sous la direction de Miescher. Il comptait 129 membres. L'Angleterre, l'Allemagne et la France avaient fourni les contingents les plus nombreux.

La brillante pleiade des physiologistes de langue anglaise y était représentée pour ainsi dire au complet: Michael Foster, Langley, Gaskell, Gotch, Bowditch, Waller, Beevor et Horsley, Halliburton. Parmi les Français: Chauveau, Arloing, Bouchard, Dastre, Morat, Gley, Lapicque, Doyon, Hédon, Arthus, Raphaël Dubois, Roger, Charrin. Parmi les Allemands: Goltz, Hermann, Heidenhain, His, Fick, Preyer, Grützner, Loeb, Rosenthal, Hering, Schiff, v. Mering, Kronecker. Parmi les Italiens: Mosso, Fano, Albertoni. Puis: Holmgren, Einthoven, Prevost, Herzen, Bunge, Kocher, Blix, Tigerstedt, Heger, etc.

On y lut peu de dissertations, mais on y fit de nombreuses expériences du plus haut intérêt. von Mering et Minkowski y démontrèrent le diabète par extirpation du pancréas. On y vit l'ergographe de Mosso, le chien sans hémisphères cérébraux de Goltz, les photographies composites de Bowditch, les variations électriques du cœur humain par Waller, la vasodilatation par excitation du sympathique cervical par Dastre et Morat. On fut émerveillée par la virtuosité opératoire des Anglais Beevor et Horsley, qui démontrèrent les fonctions motrices de l'écorce cérébrale chez le singe.

Ainsi on vit au Congrès de Bâle bien des choses intéressantes qu'on ne peut apprendre dans les livres. Ce fut aussi l'occasion pour beaucoup de physiologistes d'apprendre à se mieux connaître. Je me rappelle avoir vu à Bâle l'irascible Hering causer amicalement avec le vénérable Holmgren, contre lequel il était parti en guerre dans des termes peu parlementaires, dans *Pflüger's Archiv*. Quelques instants après, on le voyait converser avec von Kries, qui, l'année d'avant, avait déclaré, dans une autre Revue, se refuser dorénavant à toute discussion avec le Professeur de Prague.

Le succès de ce Congrès fut donc éclatant. On décida qu'on n'en resterait pas là et qu'un second Congrès se tiendrait, trois ans après, à Liège, dans le nouvel Institut qui venait d'y être construit.

Le Congrès de Liège (29-31 Août 1892) ne réunit que 102 Physiologistes. Le choléra, signalé dans différents pays, avait fait quelques victimes en Belgique, ce qui explique le nombre peu élevé des participants. Cependant les Anglais et les Français n'avaient pas eu peur du choléra et étaient venus, plus nombreux même qu'à Bâle: 25 Anglais, 20 Français.

Les traditions de "bonhomie et de simplicité monacale", le terme est de Dastre, inaugurées à Bâle, y furent strictement observées. Le Comité avait même écarté une réception officielle à l'Hôtel de ville que la Municipalité liégeoise voulait nous offrir. Tout se passa pour ainsi dire en famille. On put voir à la séance d'inauguration du Congrès, Sir Michael Foster fumant flegmatiquement sa grosse pipe, assis à la table du bureau.

Pas de réception officielle, pas de fêtes, mais du travail utile. Chauveau répéta sur le cheval vivant, ses célèbres expériences faites en commun avec Marey, sur l'enregistrement des pulsations cardiaques, au moyen des sondes cardiographiques introduites dans les cavités du cœur. Il me semble voir

encore le vénérable vieillard aux traits nobles et imposants, suivant sur l'écran mouillé, le tracé de l'oreillette et celui du ventricule, s'inscrivant l'un au dessous de l'autre. Toute la physiologie des mouvements cardiaques se déroulait devant nos yeux, interprétée avec une verve toute juvénile, chaque incident provoquant une digression et entraînant l'orateur à une nouvelle et brillante improvisation. Ce fut un moment historique, inoubliable, ce fut pour ainsi dire le *clou* du Congrès. Ces expériences impressionnèrent vivement tous les assistants, et devaient mettre fin aux controverses qu'avait suscitées en Allemagne l'interprétation des cardiogrammes et la fixation des moments d'ouverture et de clôture des valvules.

Hamburger démontra, pour les globules rouges, suspendus dans les solutions salines, les lois de l'*isotonie*, d'après la méthode de de Vries. Ces expériences, qui introduisaient la chimie physique dans les sciences médicales, ont été, comme vous le savez, le point de départ d'un nouveau chapitre de la Physiologie.

Hédon produisit son procédé de greffe sous-cutanée de la portion stomacale du pancréas, et les résultats de l'extirpation, soit du pancréas, soit du greffon, au point de vue de l'apparition du diabète. C'est l'histoire de l'*insuline* avant la lettre.

Les curieux phénomènes de l'*autotomie* des pattes y furent montrés sur des crabes vivants. Enfin on eut de nouveau l'occasion d'admirer l'impeccable habileté opératoire des Anglais, dans la personne de Sherrington, qui fit sur une guenon, l'expérience de l'excitation des centres corticaux pour l'anus et le vagin.

Le troisième Congrès s'est tenu à Berne, du 9 au 12 Septembre 1895, dans les locaux du *Hallerianum* et sous la présidence de Kronecker. Parmi les nombreuses démonstrations, mentionnons seulement l'allorhythmie cardiaque (His junior) par section du faisceau musculaire auriculo-ventriculaire, auquel on a donné depuis le nom de *faisceau de His*, la fibrillation des ventricules par occlusion des artères coronaires (Kronecker). Enfin Langley exposa ses nouvelles idées sur la constitution du système nerveux sympathique et démontra sur le chat les effets des excitations préganglionnaires et postganglionnaires.

Le Congrès de Berne, tout en étant aussi scientifique que les deux premiers, eut un caractère moins austère et un peu plus mondain: *garden party* dans la villa du professeur Kronecker, soirée offerte par le corps médical, concert d'orgue et illumination de la cathédrale, excursion à la *Schynige Platte*.

Je n'entrerai pas aussi avant dans le détail des travaux des Congrès suivants, qui se sont succédés de 3 ans en 3 ans, avec un succès et un nombre de membres régulièrement croissant, de sorte qu'au Congrès de Groningue, le dernier tenu avant la guerre, en 1913, il y avait 432 participants (voir le graphique).

Au IV^{ème} Congrès de Physiologie, tenu à Cambridge (Angleterre) sous la présidence de Sir Michael Foster, la principale innovation fut l'impression, sur feuilles volantes, du texte des communications, texte distribué aux membres du Congrès. C'est au Congrès de Cambridge qu'a été créée, sur la proposition de Marey, une *commission internationale pour l'unification et le contrôle des instruments inscripteurs en Physiologie*. C'est l'origine de l'*Institut Marey*, installé au Parc des Princes à Boulogne s/Seine, près Paris.

A Cambridge, Porter nous montra un fragment isolé de coeur de chien, nourri par une circulation artificielle de sérum oxygéné sous pression et continuant à battre. Atwater y démontra la valeur alimentaire de l'alcool, etc.

Au V^e Congrès, tenu à Turin du 17 au 21 Septembre 1901, sous la présidence de Mosso, l'italien fut adopté à côté de l'anglais, du français et de l'allemand, comme quatrième langue officielle du Congrès. On nous offrit une plaquette artistique représentant *Minerva medica*, et au banquet final on nous fit manger un chamois offert par le Roi d'Italie et tué par lui à notre intention. Dans la séance du 17 Septembre 1901, Sir Michael Foster fut proclamé *Président honoraire perpétuel* des Congrès de Physiologie.

Loeke nous montra un coeur isolé de lapin qui poursuivit ses battements pendant de longues heures, alors qu'il ne recevait comme aliment qu'une solution saline oxygénée et glycosée. Bayliss fit voir la fonction vasodilatatrice des racines rachidiennes postérieures. Langley démontra l'action paralysante de la nicotine sur les ganglions du grand sympathique.

Au VI^e Congrès, tenu à Bruxelles du 31 Août au 3 Septembre 1904, sous la présidence de Paul Heger, signalons les démonstrations d'Einthoven sur le galvanomètre à corde, de Cannon sur les mouvements de l'intestin, étudiés au moyen des rayons X, et reconstitués au moyen du zootrope, de Victor Henri sur les colloïdes, de Lapicque sur les lois de l'excitabilité électrique, de Charles Richet sur l'anaphylaxie, etc.

Le Congrès décida de prendre sous sa protection le Laboratoire du col d'Olen, à 3000 m. d'altitude et de demander au gouvernement italien de le dénommer *Institut Mosso* (ce qui fut accordé).

Le VII^e Congrès fut tenu à Heidelberg, sous la présidence d'A. Kossel, le célèbre auteur des travaux classiques sur la constitution des substances protéiques. Signalons les expériences de Bechold sur la séparation mécanique des colloïdes par l'ultrafiltration, et les communications de Delezenne, Foà, Gley, Cohnheim, Percy et d'autres, sur les ferments digestifs. On discuta un projet de classification et de nomenclature des matières protéiques présenté au nom de la *Physiological Society* de Londres.

Le VIII^e Congrès s'est tenu à Vienne du 27 au 30 Septembre 1910, sous la présidence de Sigmund Exner. Le professeur Charles Richet fit une

leçon sur *l'Humorisme ancien et l'humorisme moderne*. On commémora le 100^e anniversaire de naissance de Théodore Schwann, l'immortel auteur de la *Théorie Cellulaire*.

Le IX^e Congrès, le dernier d'avant guerre, eut lieu à Groningue, du 2 au 5 Septembre 1913, sous la présidence de Hamburger et dans le bel institut qu'on venait d'inaugurer. Pawlow y fit une conférence: *Etude expérimentale des fonctions nerveuses supérieures*.

On y admira les belles démonstrations cinématographiques de Comandon et Bull sur la pulsation cardiaque, la circulation capillaire, les mouvements du protoplasme. Mines fit voir le mouvement de contraction circulaire continu dans un anneau de tissu cardiaque et y rattacha (après Garrey 1912), une tentative d'explication de la fibrillation, etc., etc.

Si nous jetons un regard en arrière pour considérer les résultats acquis par ces neuf Congrès internationaux de Physiologie, échelonnés sur une période de 25 années, nous pouvons dire qu'ils donnent un tableau fidèle du développement et des progrès de la physiologie pendant ce quart de siècle. Ces réunions ont eu la primeur de presque tous les grands progrès réalisés dans notre science.

Elles ont constitué ainsi un précieux moyen d'enseignement mutuel pour les physiologistes: ceux-ci purent, avec un minimum de temps et d'effort, être initiés à tous les problèmes nouveaux de la science de la vie et se familiariser avec les techniques les plus diverses.

Ce fut également pour eux l'occasion d'apprendre à se mieux connaître et de nouer des relations amicales entre savants de différents pays.

Hélas! la guerre est venue interrompre cette belle tradition. Heureusement nous l'avons reprise et la continuons aujourd'hui à Boston, après Paris, Edimbourg et Stockholm.

Faisons des vœux pour la prospérité de cette oeuvre de progrès et de paix. Elle est en bonne mains, comme l'a prouvé l'éclatant succès de la présente session.

Ce succès est dû, chacun l'a compris, aux qualités exceptionnelles d'organisation du peuple américain et de ses représentants scientifiques.

MATÉRIAUX CONSULTÉS

I. Bâle, 10-12 September, 1889.

H. GAD. Centralbl. f. Physiol. 12 Oct. 1889, No. 14, p. 304.

G. GLEY, P. LANGLOIS, P. Loye et M. Baudoin, Progrès médical, 1889.

W. EINTHOVEN, Nederl. Tydschr. v. Geneesk. 1889, 2^e deel.

Allgem. Schweizer Zeitung, 1889, No. 220.

Correspondenz Blatt für Schweizer Aerzte, xix.

II. Liège, 27 Août—2 Sept. 1892.

LÉON FREDERICQ. Notice. Travaux du Laboratoire.

ALBERT RENÉ. Gazette des Hôpitaux.

- L. OLIVIER. *Rev. gén. des sc. pures et appl.* 15 November, 1892.
DR. MALBEC. *La Tribune médicale*, 1, 8 et 15 September, 1892, p. 556, 572, 587.
P. LANGLOIS. *La Semaine médicale*, No. 44, 45, 31 Août, 7 September, 1892, p. 545, 317.
P. LANGLOIS. *Revue Scientifique*, No. 11, 10 Septembre, 1892, p. 348.
M. DOYON. *Lyon médical*, No. 43, 23 October, 1892, p. 276.
J. F. HEYMANS. *Centralbl. f. Physiol.* No. 14, 8 October, 1892, p. 395.
H. J. HAMBURGER. *Nederl. Tijdschr. v. Geneesk.*, 1892, No. 12, 2^e deel.
III. Berne, 9-13 September, 1895.
A. MALBEC. *Tribune médicale*, 18 et 25 September, 1895, 762, 780.
H. BORUTTAU. *Centralbl. f. Physiol.* No. 15, 19 October, 1895, p. 465.
Correspondenzblatt für Schweizer Aerzte No. 19/21, 1895.
IV. Cambridge (Angleterre) 23-27 Août, 1898.
Résumé des communications
L. HILL. *Journ. Physiol.*, xxiii Suppl.
P. LANGLOIS. *Presse médicale*, Nos. 18-21, 28 September, 1898, p. 93.
A. DU BOIS REYMOND. *Centralbl. f. Physiol.* No. 14, 1896.
V. Turin, 17-21 Sept. 1901.
N. VASCHIDE. *Revue universelle*, 1 Fév. 1902.
H. BORUTTAU. *Centralbl. f. Physiol.* No. 17, 23 Nov. 1901, p. 479.
GIULIO FANO. *Marzocco* No. 42, 43, 20-27 Ottob. 1901.
W. EINTHOVEN. *Weekbl. v. h. Ned. Tijdschr. v. Geneesk.* No. 19. 9 Nov., 1901, p. 1090.
Z. TREVES. *Arch. ital. Biol.*
VI. Bruxelles, 31 Août-3 Sept. 1904.
A. SLOSSE. *Arch. intern. Physiol.*, ii, 1904, p. 1.
O. v. FÜRTH, A. KREIDLUND T. Nicolai. *Centralbl. f. Physiol.* 1904.
VII. Heidelberg, 13-16 Août, 1907.
LÉON FREDERICQ ET PAUL HEGER. *Arch. intern. Physiol.*, 1907, v.
VIII. Vienne, 27-30 Sept. 1910.
LÉON FREDERICQ. *Arch. intern. Physiol.*, x, Oct. 1910.
O. v. FÜRTH ET A. KREIDL. *Zentralbl. f. Physiol.*, No. 17, 1910, p. 780.
IX. Groningue, 2-5 Sept. 1913.
LÉON FREDERICQ ET PAUL HEGER. *Arch. intern. Physiol.*, xiv, Oct. 1913.
H. J. HAMBURGER ET ERNST LAQUEUR. *Testsschrift zum 25 jähr. Gedenktage der Gründung der intern. Physiologen. Kongresse. Zentralb. f. Physiol.*, Groningen, 1913.
G. VAN RYNBERK. *Le Congrès intern. des Physiol. à Groningue. Nederl. Tijdschr. v. Geneesk.* 30 Aug. 1913 *Weekblad*, No. 9, *Tweede Helft*.

ABSTRACTS OF COMMUNICATIONS TO THE THIRTEENTH
INTERNATIONAL PHYSIOLOGICAL CONGRESS

ABDERHALDEN, E. (HALLE). **Forschungen über das Wesen von Fermentwirkungen.**

Die Beobachtung, dass Polypeptide, die bei bestimmtem pH und bei bestimmter Temperatur innerhalb einer bestimmten Zeit entweder gar nicht aufgespalten werden oder aber einer Hydrolyse unterliegen, unter den gleichen Bedingungen zur Aufspaltung kommen bzw. ausserordentlich viel schneller hydrolysiert werden, sobald die freie Aminogruppe des Polypeptids durch bestimmte Gruppen z. B. die Phenylisocyanatgruppe besetzt wird, hat zu der Vorstellung geführt, dass der Fermentwirkung die Bildung einer Zwischenverbindung zu Grunde liegt, und zwar erfolgt die Bindung der Fermentgruppe an eine bestimmte Atomgruppierung im Substrat. Für die Bildung dieser Verbindung dürfte eine bestimmte Wasserstoffionenkonzentration von massgebender Bedeutung sein. Das entstandene Produkt ist gegenüber der freien Verbindung weitgehend in seinen inneren Strukturverhältnissen beeinflusst, so dass nunmehr die vorhandene Wasserstoffionenkonzentration zur Herbeiführung einer Hydrolyse ausreicht. Nach dieser Vorstellung müsste im Sinne von Emil Fischer das Ferment über Atomgruppierungen verfügen, die ihrer ganzen Anordnung und Wirkung nach so beschaffen sind, dass eine Bindung mit einer bestimmten Atomgruppierung im Substrat ermöglicht wird. Der Umstand, dass bis jetzt kein Polypeptid von Erepisin zur Aufspaltung gekommen ist, in dem die freie Aminogruppe besetzt war, spricht dafür, dass die genannte Fermentgruppe Beziehungen zur genannten Gruppe besitzt. Trypsin dagegen scheint als Verankerungsstelle die freie Carboxylgruppe der Polypeptide zu haben.

ACHELIS, JOHANN (LEIPZIG). **Über Reizversuche mit Wechselströmen niedriger Frequenz.**

Am Nervmuskelpreparat des Frosches werden mit *sinusreinen* Wechselströmen von 15-600 Hertz Schwellenbestimmungen durchgeführt. Der verwendete von Gildemeister konstruierte Generator für 15-50.000 Hertz, und die Methode der Intensitätsmessung wird kurz beschrieben. Die Ergebnisse sind folgende: Es gibt für den motorischen Nerven bei Zimmertemperatur eine deutliche Optimalfrequenz, d. h. eine Frequenz, bei der die Reizung mit einer minimalen Intensität möglich ist. Oberhalb und unterhalb dieses Optimums steigen die Schwellenintensitäten wieder an. Die Lage dieses Optimums ist für verschiedene Fasern des Nerven verschieden. Unter gewissen Bedingungen lassen sich Strecker und Beuger nach Lage ihres Optimums unterscheiden. Das Optimum verschiebt sich bei Abkühlung zu niedrigeren Frequenzen.

Die beiden Teile der Schwellenkurve verhalten sich bei Temperaturwechsel *entgegengesetzt*. Der Kurventeil für niedrige Frequenzen (Optimum) ist *sehr* temperaturabhängig, die Schwellen *sinken* bei Abkühlung.

Der grosse Temperaturkoeffizient für die Schwelle bei niedrigen Frequenzen und der entgegengesetzte geringe für höhere Frequenzen weisen auf eine notwendige Korrektur der Reizgesetze hin, die aber bisher nur qualitativ formuliert werden kann.

ADDISON, W. H. F. (PHILADELPHIA). **The Normal Histology of the Standard Albino Rat at 150 Days of Age Illustrated by 100 Photomicrographs. (Demonstration)**

ADLERSBERG, D. (WIEN). **Über das Wesen der sogenannten Gallenblasenreflexe.**

Beim Menschen gelingt es auf zweierlei Art den sogenannten Gallenblasenreflex auszulösen, d. i. dunkelgefärbte, konzentrierte "Blasengalle" mit Hilfe der Duodenalsonde zu gewinnen: 1. Durch intraduodenale Zufuhr von konzentrierter Magnesiumsulfat-Lösung, ferner Wittepepton-, Glukoselösung. 2. Durch parenterale, in der Regel subkutane Applikation von Pituitrinpräparaten, von Ergotamin und Pilocarpin. Als Vertreter der ersten Gruppe wurde der Magnesiumsulfat-, als Vertreter der zweiten der Pituitrinreflex näher untersucht.

Die tägliche klinische Beobachtung legt den Gedanken nahe, dass es sich hier um zwei verschiedenartig ausgelöste Einwirkungen auf das gleiche Organ handelt. Während der Magnesiumsulfatreflex nach ganz kurzer Zeit auftritt, zeigt der Pituitrinreflex eine längere oder kürzere Latenzzeit. Der Magnesiumsulfatreflex scheint somit ein *kurzer* Reflex zu sein, der durch eine direkt vom Duodenum auf die Gallenblase sich fortpflanzende Erregung zustande kommt, der Pituitrinreflex dagegen auf dem Wege einer *langen* Reflexbahn zu erfolgen. Dieser Gedanke konnte durch klinisch-experimentelle Untersuchungen gestützt werden.

Bei normalen Versuchspersonen, die nach Zufuhr von Pituitrin allein den typischen Gallenblasenreflex zeigten, konnte durch eine der Pituitrininjektion vorangehende Darreichung von Narkotieis der Hirnstamm-Gruppe (Luminal, insbesondere aber Chloreton) eine wesentliche Abschwächung und Verzögerung, vielfach vollständiges Fehlen der Gallenblasenentleerung beobachtet werden. Hingegen zeigte ein Vertreter der Hirnrinden-Narkotica (Paraldehyd) diese Wirkung nicht. Der Magnesiumsulfatreflex wird hingegen durch das Hirnstamm-Narkotikum Chloreton in keinerlei Weise beeinflusst. Die lange Reflexbahn der Pituitrinwirkung auf die Gallenblase dürfte somit gewisse Stellen des Hirnstammes passieren, deren Funktion durch die Wirkung der Hirnstamm-Narkotika eine Veränderung erfährt. Dass für das Zustandekommen des kurzen, direkt erfolgenden Magnesiumsulfatreflexes Einwirkungen dieser Art bedeutungslos sind, stützt ebenfalls die oben erwähnte Hypothese.

Schliesslich zeigten unter 8 Fällen mit Erkrankung des Hirnstammes 2 Fälle von postencephalitischem Parkinsonismus bei mehreren Untersuchungen Fehlen des Pituitrinreflexes bei prompter Auslösbarkeit des Magnesiumsulfatreflexes. Diese Erscheinung wird im gleichen Sinne durch veränderte Funktion gewisser im Hirnstamm lokalisierter Stellen erklärt. Es müsste somit in Zukunft in der Klinik bei Fehlen des Pituitrinreflexes neben einer Erkrankung der Gallenwege (Cholelithiasis-Verschluss, Schrumpfung der Gallenblase u. dgl.) auch die Möglichkeit einer zentral erfolgenden Hemmung in Erwägung gezogen werden.

ADOLPH, EDWARD F. (ROCHESTER, N. Y.). **How the Skin Equilibrates the Water Content and the Osmotic Pressure of Frogs.**

What forces governing water exchanges enable frogs to live in balance with a medium of zero concentration? To evaluate the factor of osmotic pressure, *Rana pipiens*, with cloacae bound to prevent loss of urine, were transferred from water to various concentrations of NaCl, and their changes of water content were measured by weighing. The initial rates at which water then passed through the skin were proportional to the concentration in all hypertonic solutions but not in hypotonic ones. When transferred from one concentration of NaCl to another, the average rates were in each case the algebraic sum of those rates found after transfer from water to each of the two concentrations.

Other frogs from which the skin was completely removed were placed in various concentrations of NaCl. The initial rates of water passage were now proportional to the concentration throughout the whole range of solutions. In the hypertonic ones the rates were about three times as great as in intact frogs, corresponding to the relative thicknesses of tissue through which water had to diffuse between medium and circulating blood.

Isolated skins likewise swelled in proportion to the dilution of the medium, and the same is known to be true for isolated muscles.

When intact frogs were transferred to any hypotonic medium, the initial entrance of water due to osmotic pressure was evidently opposed, and to a greater extent in the greater dilutions up to pure water. Since without the skin this opposition was absent, the force residing in the skin may be evaluated, at each concentration of the medium, by subtracting the rate of passage of water into the normal frog from the rate which would prevail if the skin were absent yet the diffusion rate were always proportional to osmotic pressure. The opposing or non-osmotic force is thus found to be approximately proportional to the reciprocal of the external concentration, being insignificant in any hypertonic medium.

ADRIAN, E. D. (CAMBRIDGE) and D. W. BRONK (PHILADELPHIA). **The Electric Response in Small Groups of Muscle Fibres. (Demonstration)**

Concentric needle electrodes lead from a restricted group of muscle fibres to the input of a three valve amplifier. The amplified action potentials are then transformed into sound waves by means of a second power amplifier and loud speaker. It is thus possible to follow by ear the frequency of the impulse discharge during a voluntary contraction.

AGDUHR, ERIK (UPSALA). **Cod-Liver Oil in Therapeutic Doses Causes Organic Changes.**

I am presenting to you changes which occur following prolonged feedings with cod liver oil.

The changes are principally of three kinds:

I. Decreasing weight curves

II. Electrocardiographic changes and

III. Histological changes in different organs chiefly of regressive type.

Eight years ago in trying to find out a diet for experimental animals which should be capable of producing a specially strong post natal development I added cod liver oil (c. l. o.) to the food of several groups of white

mice. Two of these groups (10 animals in each group) received c. l. o. (about 5 cc. kg./day) and basal diet while an equal number of mice received the basal diet only. The basal diet of one group was composed of rye-bread, milk and oats while the other group received the "complete diet" of vitamin-researchers consisting of casein, fats, starch, yeast, orange juice and mineral salts.

The weight curves of the mice as well as the microscopical examination of their organs (after the experiments had been going on for a year) showed many disturbing alterations in the animals which had c. l. o. added to their food. At this time I did not publish my observations though everything indicated the c. l. o. as the cause of these alterations. Since c. l. o. enjoys such a high reputation as a vitamine-containing medicine, and in many places also as an easily digested food, it seemed necessary to make further investigations concerning these matters.

Failing in my endeavors to arouse the interest of others in the problem of the injurious effects of c. l. o. I undertook a systematic investigation of it myself, although it lay considerably outside the scope of my usual studies.

Up to now these experiments of mine embrace more than 1400 animals, to which belong white mice (the greatest number) white rats, rabbits, calves, pigs, cats and dogs—besides which I have also had the opportunity of making a microscopical examination of some organs belonging to two children, which had been subjected to c. l. o. medication.

All the series have of course been accompanied by control-animals. Within one and the same series the different groups of animals have received the same basal diet, but their doses of c. l. o. have been different—they have corresponded to 0.1 cc., 1 cc. or 5 cc. per kg. bodyweight a day (kg./day).

C. l. o. of the best quality which is to be purchased in Sweden, Norway, as well as in several other countries and which is dosed in the quantities mentioned can cause lesions in most of the organs of the animals in question.

The smaller the dose of c. l. o. and the more "complete" the basal diet of the animal, the longer it takes to produce these lesions.

C. l. o. administered as an emulsion with gum-arabic or as grasiol has a more injurious influence on experimental animals (white mice) than corresponding doses of pure c. l. o. In these animals disturbances in the function of the heart may sometimes be proved electrocardiographically a fortnight after the beginning of the experiment.

The susceptibility in regard to the toxic action of c. l. o. varies very much in different individuals of the same species of animal, and different species of animals also show varying susceptibility if measured by the standard "Like effects from like quantities of c. l. o. per kg. bodyweight."

A medication with c. l. o. for a sufficiently long time causes a decrease of the normal weight-curve of the animals, but even during the early period of life when the weight-curves are strongly increasing very pronounced organic lesions (f. ex. heart-lesions) may appear (f. ex. in calves and pigs).

Large doses of c. l. o. have as a rule been followed by a decrease in the number of *red blood corpuscles* simultaneously with a fairly steady increase of the relative haemoglobin value. C. l. o. exercises a considerable irritative action on the red bone-marrow, there leading to an increased formation of new cells during a rather long period thereby causing the appear-

ance of a much larger number of erythroblasts in the blood than is usually the case. The disintegration of the red blood-corpuscles, however, also seems to take place more rapidly than usual, so that the number per mm.³ frequently diminishes after a period of dosing. *The white blood-corpuscles* show almost without exception an increase in number in the beginning. This increase is—in all the animals studied except the calves—for the most part due to an increase of the polymorph-nuclear leucocytes, dependant on the irritation of the red bone-marrow. In calves it is the lymphocytes that increase simultaneously with the diminution in number of the polymorph-nuclear leucocytes. If c. l. o. dosing be continued for a sufficient length of time leucocytosis disappears and is followed by leucopeni. The blood-platelets usually increased considerably in number. This thrombocytosis continued in several animals throughout the entire experimental period; in others the number of blood-platelets sank after a time to the normal, while in some animals a considerable thrombopeni arose as well. Several of the latter animals showed hemorrhage, inter alia, in the myocardium. C. l. o. acts more powerfully on the blood-picture in the direction mentioned when applied subcutaneously and intraabdominally than when given per os.

In calves the lymphoidal tissues of the intestine showed considerable hypertrophy—Tayer's plaques being many times larger than usual. The red bone-marrow of many animals studied was visibly hypertrophied, looking dark through the comparatively thin cortex. After a lengthy treatment with c. l. o. several signs of disintegration appeared in the blood-cell-forming elements.

The spleen is often abundantly supplied with blood-pigments, a sign that the disintegration of the red blood-corpuscles is above the normal. The parenchyma, specially the lymphocytes, is in many cases injured and destroyed so that the stroma distinctively emerges.

In the adrenal glands pigment-atrophy has appeared with great regularity even from comparatively small doses—especially in white mice.

In animals whose kidneys showed morphological changes, it generally has been a case of nephroses. In some cases there have been considerable accumulations of pigment in the epithelial cells of the tubules.

Among other lesions miliary hemorrhages also sometimes occur in the mucosa of the stomach and intestine. The changes in the digestive tract are not infrequently connected with more or less severe icterus, occasioned by the c. l. o.

Not infrequently the liver, the lungs, the nerve system and the skeleton also showed different types of regressive changes.

In cross-striated muscle (including the heart-muscle) such changes as calcareous incrustations, simple atrophy, vacuolous degeneration, pigment-degeneration, fatty degeneration, transformation into connective tissue etc. are fairly common.

The electrocardiographic alterations, however, in comparison with the morphological ones, are usually not very prominent, nor is this to be expected considering the mechanism of the Ecg. and the nature of the morphological injury. Thus it is hardly possible to ascertain from a single electrocardiographic record if alterations of the heart really are present. Repeated examinations of the Ecg., however, reveal in nearly all cases the progress of obvious and even very prominent alterations in the mechanism of contraction of the heart.

The alterations of the Ecg. occur at different times according to the dose of oil, but even such small amounts of c. l. o. as 0.1 cc. per kg./day produce very obvious alterations in less than a year.

An addition of lemon juice (up to 10 cc. kg./day), marmite (up to 10 cc. kg./day), or marmite and lemon juice cannot protect the experimental animals (rabbits) against the toxic influences of c. l. o.

In 1926 I stated that white mice on full diet showed better generative faculty than others which, in addition to the same basal diet, were given c. l. o. Cats and dogs, which from the age of one month had been included in the experimental series (1 cc. c. l. o. per kg./day) for a year, showed no signs of heat during this period, and attempts at pairing also failed. On the other hand, a bitch taken into the series of experiments after reaching maturity gave birth to five pups four months after the start of the experiment but later on showed no further signs of heat.

The female generative organs of the dogs in question showed advanced regressive changes; retardation in the normal post-natal development of the germinal cells (with numerous instances of more than one ovum in the same follicle—up to eight ova are counted in one simple 10μ section of the same Graaf's follicle), highly degenerative fatty infiltration not only in a great number of the cells of the ovary but also in the epithelium cells of the mucous membrane of the uterus, purulent catarrh in the vagina and the vestibulum.

In mice, previously treated with emulsion of c. l. o. for 3 to 5 months a study was made of the appearance of the Ecg. for the following 7.5 months without cod liver oil as well as of the morphology of the hearts of these animals when killed.

The Ecg. appears gradually to regain the normal state. Complete restitution, however is not attained—and while the anatomical lesions of the heart are in general less prominent in the animals which had been for several months without c. l. o., nevertheless no examples of the complete anatomical healing of these lesions has been observed.

Which of the constituent parts of the c. l. o. are responsible for its toxic effect?

Several substances isolated from c. l. o. or developed in other ways (Dr. G. Blie) and dosed to mice in the same quantity as they exist in a dose of c. l. o. corresponding to 5 cc. per kg. day have caused organic lesions. Among such substances may be mentioned ergosterin and cholesterin (radiated or not radiated with ultraviolet light) as well as unsaturated fatty acids. The more nearly the artificially prepared substances represent the original c. l. o., the more closely the lesions produced resemble those caused by c. l. o.

The effect of summer sunlight or a not too strong radiation with ultraviolet light (up to 10 minutes daily at a distance of 80 cm.) seems to increase the resistance offered by animals to the toxic property of c. l. o. A too strong radiation (f. ex. 60 minutes daily for several months and at a distance of 50 cm.), however, causes organic lesions itself.

ALLEN, FREDERICK M. (MORRISTOWN, NEW JERSEY). Vicarious Function of the Sweat Glands for the Kidneys in Nephritis.

Dry heat, which is recognized as less debilitating than humid heat, can be used in suitable nephritic cases to produce 4 liters or more of perspiration daily over long periods without the prostration which impaired the useful-

ness of former methods. Some of the observations made in this work are as follows:

1. The chief nitrogenous constituent of the sweat is urea, which may rise above 1000 mg. per cent. Creatinine has been found to about 12 mg. per cent. Aromatic substances (indican, were found not present, or only in traces.
2. The concentration of the above substances in the sweat is governed chiefly but not wholly by the concentration in the blood.
3. The chief inorganic constituent of the sweat is NaCl, often above 200 mg. per cent. Phosphates appear in very low values.
4. The NaCl concentration in the sweat is not parallel to that in the blood, but apparently governed more by other factors.
5. The vicarious function of the skin for the kidneys by the new dry heat treatment can reduce the blood urea to degrees never before demonstrated, *e.g.*, from 180 mg. to 60 mg., and in some cases of chronic nephritis this improvement can be long maintained.
6. Symptoms are correspondingly relieved, confirming the conception of uremia as due to retention.
7. The clearing up of edema by the dry heat is also powerful. This is physiologically important in relation to the conception of the "Vorniere" or tissue retention.
8. Hydremia can also be reduced; *e.g.*, plasma volume from 4570 cc. to 3875 cc.
9. Blood pressure is relatively little affected, the rise or fall in short treatments being usually slight.
10. Cardiac weakness usually does not contraindicate the treatment, but limits are imposed by the special vascular abnormalities present in many cases of nephritis and hypertension. In severe cases only brief sweating can often be tolerated. In the severest cases the use of heat may be inadvisable because of collapse, or may produce fever instead of sweating.

ALPERN, DANIEL (KHARKOW). Das Viszeralnervensystem als Regulator des Gewebismetabolismus.

Im Laufe der letzten Jahre studierte ich gemeinschaftlich mit meinen Mitarbeitern¹ das Problem der Abhängigkeit des Gewebsstoffwechsels von der Funktion des Viszeralnervensystems. Experimente wurden am ganzen Organismus angestellt und bezogen sich entweder auf den Gesamtorganismus oder, meistens, auf einzelne Organe, deren vegetativer Innervationsmechanismus vollständig bekannt ist. Aus den zahlreichen Versuchen an Drüsenorganen erhellte Folgendes: 1) Im Gegensatz zu dem parasympathischen System waltet das sympathische System allein über die nutritiven Prozesse im Drüsengewebe, indes es sowohl die Wechselbeziehungen der Salze in demselben, als auch den Stickstoffhaushalt reguliert; 2) Der Mechanismus eines solchen Einflusses wird durch Regelung der sog. Zellpermeabilität vor allem bewerkstelligt und 3) diese Eigenschaft des sympathischen Nervensystems darf nicht allein auf die Beeinflussung der Gefäßwandung zurückgeführt werden, es muss vielmehr als Tatsache anerkannt werden, dass der Gewebismetabolismus von ihm direkt geregelt wird. Dies wurde auch an einer Reihe von Untersuchungen bestätigt, die an desympathisierten Muskeln sowohl unter physiologischen als auch unter pathologischen Bedingungen im Organismus unternommen wurden; im chronischen Experiment trat die Bedeutung des Viszeralnervensystems für den Chemismus des Muskelgewebes noch deutlicher hervor. Weiterhin erwies eine Reihe pathologischer Vorgänge,

¹ von Besunly, Gaissinsky, Kaminsky, Lewantowsky, Lindenbaum, Tutkewitsch.

z. B. das Fieber und die Entzündung-namentlich diese letztere-mit voller Klarheit die Rolle des sympathischen Nervensystems, da eine Funktionsstörung dieses letzteren ein Kausalmoment in der Störung der Gewebsernährung darstellt, welch letztere den Beginn des Entzündungsprozesses charakterisiert.

Endlich sieht man auch an Kranken mit einseitiger Störung der viszeralen Innervation (hauptsächlich bei Syringomyelitikern), bei denen die Funktionsstörungen des sympathischen Nervensystems einseitig lokalisiert sind, Anzeichen einer chemischen Störung in dem von der betroffenen Extremität abfließenden Blute, wenn man dasselbe mit der Kontrolle vergleicht (Ergebnisse der Untersuchungen des von den oberen Extremitäten abströmenden Blutes auf Elektrolyte, Lipide, Zucker u.a.).

Somit ist die sog. *vegetative Assymetrie der Gliedmassen* offenbar in einer deutlich wahrnehmbaren *chemischen Assymetrie* begründet.

Dies alles gestattet die regulierende Einwirkung des *sympathischen Nervensystems auf den Gewebsmetabolismus* als eine erwiesene Tatsache zu betrachten, die die Einheitlichkeit der im Organismus sich abspielenden Prozesse sowohl im normalen, als auch in pathologischen Zuständen sichert.

AMBERG, SAMUEL (ROCHESTER, MINNESOTA). **Demonstration of Filtration Through the Living Mesentery of the Rabbit.** (Demonstration)

AMBERSON, WILLIAM R. (PHILADELPHIA). **Persistent Electrical Effects in Nerve Following the Application of One or Two Stimuli.**

Photographic records of the deflection of a Downing moving-magnet galvanometer, operated at high sensitivity and short period (0.6 to 1.5 sec.), show that, following the application of a single electrical stimulus, or two stimuli at short intervals, the electrical response from both amphibian and mammalian nerve gives a form of deflection which is quite different from that produced by break induction shocks from a coreless coil in which the duration of potential is very brief. Under a variety of conditions the time to maximum deflection is considerably longer (0.1 to 0.3 sec.) for the nerve than for the physical control. This is believed to indicate the presence, in the single action potential wave, of a persistent low-voltage retention of negativity. When two stimuli are applied a summation of the persistent elements can be demonstrated. Previous activity markedly increases the magnitude and duration of the effect. Under certain conditions the negative retention may be succeeded by an "after-positivity." Retentions, either positive or negative in sign, may often be found to persist for some seconds.

ANDRUS, E. COWLES and EDWARD P. CARTER (BALTIMORE). **A Device for Determining the Refractory Period of the Mammalian Heart during Normal Sinus Rhythm.** (Demonstration)

An apparatus will be demonstrated which utilizes the action current after amplification to make it possible to interrupt the sinus rhythm at any interval following a normal excitation. The amplifier is designed to be connected to the terminals of the galvanometer string without affecting the performance of the latter. The electric impulse to be amplified is on the order of 1 millivolt for $\frac{1}{100}$ second, and the current supplied to the amplifier must be negligible as compared with about 1 microampere,

the galvanometer current. A 5-stage, resistance-coupled amplifier is used, with 4 UX-240 tubes and 1 UX-112 A. The string terminals are connected directly in the first grid circuit. The 4 coupling condensers are large, so as to give the entire amplifier a discharging time constant of $\frac{1}{8}$ second. The first 2 plate circuits have condensers in parallel, so as to obtain a charging time constant of $\frac{1}{50}$ second. In this way the amplifier is rendered free from impulses of much longer or shorter duration. A 10,000-ohm magnet carries the plate current of the last tube, normally less than $\frac{1}{2}$ milliamperes because of a large negative grid voltage. An impulse of $\frac{1}{2}$ millivolt for $\frac{1}{50}$ second, applied to the amplifier, is amplified to over 20 volts for $\frac{1}{50}$ second at the magnet terminals, about 200,000 times the applied impulse.

The only adjustments in operating the amplifier are: a parallel resistance to adjust the applied impulse to about 1 millivolt, and a reversing switch to secure the correct polarity. A switch in parallel with the magnet, when closed, allows any adjustments while observing the deflections of a milliammeter in series—without actuating the magnet. On the second impulse after opening this switch, the magnet, through an escapement, releases a falling arm which, in turn, opens a trip-switch, breaking the primary circuit of an induction coil. Operation on the second impulse eliminates errors which might otherwise enter if the switch is opened during the first impulse. The trip-switch is opened after a delay of $\frac{1}{20}$ to $\frac{1}{2}$ second, depending upon the position of adjustable weights on the falling arm.

The authors wish gratefully to acknowledge the assistance of Dr. H. A. Wheeler of the Department of Physics, Johns Hopkins University, in designing and constructing this apparatus.

ANDRUS, E. COWLES and EDWARD P. CARTER (BALTIMORE). Observations upon the Refractory Period of the Normally Beating Mammalian Heart.

Previous determinations of the refractory period of the mammalian auricle have involved driving the heart with a series of break induction shocks at a rate necessarily more rapid than that of the spontaneous rhythm. The local stimulating effect of these repeated shocks has made accurate measurements possible only upon the atropinized heart, and in many instances, has led to false responses.

Using a specially designed apparatus, described in the *Proc. Soc. Exp. Biol. and Medicine*, 1928, xxv, 695, the authors have determined the refractory period of the normally beating dog's heart. The action current is led off from the auricle, amplified to 12–20 volts, and applied to a light relay. Activation of the relay releases a pendulum which in turn throws in a single break induction shock at an interval controlled by the position of a tumble switch along its arc. By this means the normal excitatory process is utilized to control the timing of the interrupting shock. In contrast to earlier measurements the results of the authors show a sharp point above which each stimulus produces a response and below which excitation fails to occur.

A series of measurements has been made under a variety of conditions. The refractory period of the normal dog's auricle has been found to lie between 0.09 and 0.12 sec. Stimulation of the vagus brings about con-

spicuous shortening to 0.05 or even less. A single dose of atropine sufficient to paralyse the vagus causes the refractory period to lengthen. Slow intravenous infusion of adrenalin produces considerable shortening but not to the extent produced by vagus stimulation.

Finally it has been repeatedly observed that under vagus stimulation a single stimulus, introduced on the auricular appendix just after the end of refractory period is followed, not by a single response, but by auricular fibrillation. The fact that under conditions of increased vagus tone, an extrasystole, occurring early in diastole may lead to a re-entrant rhythm, is, it seems, significant as a possible explanation of the genesis of auricular fibrillation.

ARTOM, CAMILLO (PALERMO). Effetti del raffreddamento dei gangli nervosi.

L'A. si è proposto di studiare in un animale omeotermo (gatto) gli effetti del raffreddamento di gangli nervosi, di differente significato anatomico e funzionale (gangli simpatici e gangli spinali od omologhi agli spinali) in condizioni di esperimento tali da permettere una diretta comparazione fra gli effetti del raffreddamento del ganglio e quelli di un identico raffreddamento, portato sulle fibre nervose pre-e post-gangliari.

Dai risultati sperimentali ottenuti, appare che:

1°. Il raffreddamento progressivo del ganglio cervicale superiore o del tronco del simpatico cervicale determina una progressiva diminuzione della eccitabilità di soglia per la dilatazione pupillare. Tale diminuzione, per abbassamenti identici di temperatura, avviene in misura più cospicua, quando si raffredda il ganglio, che non quando si raffredda il nervo. Il blocco della conduttività si ottiene, in maniera rapida e reversibile, per un raffreddamento intorno a 15°C. a livello del ganglio cervicale superiore, mentre la sospensione (egualmente reversibile) della conduzione nervosa nelle fibre (pregangliari) del simpatico cervicale non è raggiunta che con un raffreddamento molto più intenso del tronco nervoso (fra 7° e 4°C.). Le curve, esprimenti le variazioni della eccitabilità di soglia in funzione della temperatura, a cui è portato il ganglio cervicale superiore, sono leggermente diverse, a seconda che la temperatura sia fatta variare in senso discendente, ovvero in senso ascendente, dopo permanenza del ganglio per un certo tempo a bassa temperatura (isteresi termica del ganglio).

2°. Anche il ganglio stellato presenta una labilità al raffreddamento considerevolmente maggiore di quella che dimostrano le fibre (post-gangliari) dei nervi acceleranti cardiaci, le temperature di blocco della conduttività essendo di circa 15° per il ganglio e poco sotto 6° per le fibre nervose.

3°. Sottoponendo a raffreddamento il ganglio giugulare del vago (omologo ad un ganglio spinale) e un segmento del vago al collo, la conduzione degli eccitamenti centripeti, determinanti modificazioni del ritmo respiratorio, è abolita solo per un raffreddamento poco sopra lo 0°, e in modo praticamente identico, sia che il raffreddamento agisca sul ganglio, sia che agisca sul tronco nervoso.

4°. Parimenti, il blocco della conduttività per stimoli, determinanti reazioni riflesse del padiglione auricolare e dei muscoli facciali, si ottiene per un raffreddamento del nervo grande auricolare e del 2° ganglio cervicale (spinale) poco sotto 7°5, e senza che siano sicuramente rilevabili differenze

fra gli effetti del raffreddamento del ganglio e quelli del raffreddamento del nervo.

I gangli simpatici presentano dunque una labilità al raffreddamento considerevolmente maggiore che non le fibre nervose e i gangli spinali (od omologhi agli spinali). In realtà per questi ultimi il blocco della conduttività si ottiene a temperature differenti (fra 7° e 0°), ma le differenze rientrano nell'ordine di quelle osservate fra le temperature di abolizione della conduttività nei differenti tronchi nervosi di animali omeotermi.

Nei gangli simpatici invece la sospensione reversibile della conduttività si ottiene per un abbassamento termico molto meno considerevole (intorno a 15°C).

Da questo punto di vista, l'azione di questo raffreddamento di modico grado può essere paragonata all'azione farmacologica della nicotina, che, in dose appropriata, determina la interruzione della conduttività a livello del ganglio simpatico, mentre rimane senza effetto sulle fibre nervose e sugli elementi cellulari del ganglio spinale. In analogia appunto con l'interpretazione proposta per quanto riguarda l'azione della nicotina, si può pensare che la particolare labilità al raffreddamento dei gangli simpatici dipenda dalla presenza in essi della "sinapsi interneuronica": l'interruzione della conduttività a livello dei gangli simpatici sarebbe l'espressione di mutamenti dei componenti colloidali della sinapsi, mutamenti dotati di alto coefficiente termico e reversibili con la successiva rilevazione della temperatura.

Concorrerebbero ad avvalorare tale ipotesi i risultati di alcune esperienze relative alla maggiore labilità al raffreddamento delle giunzioni neuromuscolari in confronto del nervo e del muscolo.

ASHER, LEON (BERN). Das Verhalten des Kreislaufs und des Zentralnervensystems des Säugetieres bei hochgradigem Sauerstoffmangel.

Der Nachweis, dass die Automatie des Kaltblüterherzens und eine genügende Leistungsfähigkeit bei vollständigem Ausschluss von Sauerstoff drei Tagelang erhalten bleibt, wenn für physiologische Bedingungen gesorgt wird, regte eine erneute Prüfung der Frage an, ob nicht für das Säugetierherz Bedingungen gefunden werden könnten, unter denen es selbst bei hochgradigem Sauerstoffmangel, leistungsfähig blieb. Es wurde eine Methode ausgearbeitet, um den auf Grund theoretischer Erwägungen postulierten Bedingungen zu genügen. Die Methode besteht aus einem neuen Verfahren der künstlichen Atmung, durch welche dem Kaninchen aus einem Gasometer sauerstoffarme Luft zugeleitet wird und die Lungen ventiliert werden unter gleichzeitiger Massage der Herzgegend und aus einem Dauereinlauf von Adrenalin, um selbst bei gelähmtem Vasomotorenzentrum einen guten Kreislauf aufrecht zu erhalten. Demonstration der Apparatur durch Diapositive.

Bei erzwungener Einatmung einer Luft mit nur 4,2 Procent Sauerstoff wird das Blut rasch asphyktisch, Krämpfe brechen aus, die vergehen, und nach etwa 15 Minuten verschwinden die Reflexe und die Aeusserung einer Spontanatmung. Herz und Blutdruck bleiben stundenlang in gutem Zustand. Hört man mit der künstlichen Atmung auf, so beginnen etwa nach einer Minute spontane Atmungen und bei Andauer der Adrenalininfusion bleibt Atmung und Kreislauf in gutem Zustand.

Zwischen 4,2 und 4 Procent Sauerstoff bleibt der Herzschlag nur 15 Minuten lang in gutem Zustand. Auch hier erholt sich spontan das

Atemzentrum. Beim Tier mit verkürztem Kreislauf wird stundenlang ein guter Kreislauf beobachtet bis zu einem Sauerstoffgehalt bis zu 3,75 Procent. Auch hier erholt sich das Atemzentrum. Die Versuche zeigen, dass bei dauernder kräftiger Entfernung der Kohlensäure und Aufrechterhaltung guter Kreislaufsbedingungen durch Adrenalin das Säugetierherz und das Atemzentrum gegen grossen Sauerstoffmangel sehr resistent sind.

ASHMAN, RICHARD and ROBERTA HAFKESBRING (NEW ORLEANS). **Unidirectional Block in Heart Muscle.**

By proper local compression of a ventricular strip from the turtle (*Emys blandingii* or *Chelydra serpentina*) it is possible to control the direction of irreciprocal conduction. For this purpose the strip, laid horizontally upon a flat surface, was compressed near its center beneath a rubber stopper inserted into the end of a vertical glass tube. The surface of the stopper in contact with the muscle was plane, rectangular, and inclined at an angle of about 10° with the horizontal. Thus the edge of the underlying region which faced one end of the muscle was more strongly compressed than the opposite edge. Electrical stimuli were applied alternately at either end of the strip while the compressing force was gradually increased by the addition of weights to a box resting upon the upper end of the tube. The electrical responses of the ends of the strip were recorded. Block usually first appeared when the impulse was required to travel through the compressed region in the direction from lighter to stronger compression. Only after the application of additional weight, equaling, on the average, 28 per cent of the total, did block supervene in both directions. This was the result in 30 experiments. In 21 trials, the onset of block in the two directions was practically simultaneous. In only two cases did block first occur in the direction opposite to the usual. In 7 strips the direction of initial block was changed by reversing the orientation of the compressor. In general, before unidirectional block supervened, conduction became slower in that direction than in the opposite. In the majority of cases, when there was recovery from complete block, the first return of conduction was in the expected direction.

These results demonstrate the correctness of Engelmann's¹ generalization, namely, that the impulse is transmitted more readily from a region of high excitability (or conductivity) to one of low excitability than in the reverse direction.

ASZÓDI, ZOLTÁN (BUDAPEST). **Über den Schwefelgehalt der Eiweisskörper im Blutserum verschiedener Warmblüter.**

Angesichts der einander widersprechenden Angaben der Autoren über das Globulin im Blutserum, über verschiedene Modifikationen desselben, über die Möglichkeit letztere durch Ausfällen unter verschiedenen Versuchsbedingungen von einander zu trennen, über ihre Individualität als wohldefinierte chemische Verbindungen, war eine Klärung dieser Fragen von einer Bestimmung des Schwefelgehaltes mittels einer Methode zu erwarten, die leicht handlich ist, dabei aber auch an wesentlich geringeren Substanzmengen, als es die älteren Methoden gestatten, gute Resultate liefert. Eine solche Methode ist die von ter Meulen (Glühen des zu untersuchenden

¹ Pflüger's Arch., 1896, lxii, 400.

Stoffes in H-Athmosphäre, Auffangen des H_2S in das der gesamte Schwefel verwandelt wird in Lauge, jodometrische Bestimmung). Von dieser Methode war umso eher Verlässliches zu erwarten, da mit ihrer Hilfe erst jüngst festgestellt werden konnte, dass die Hämoglobine verschiedenen Ursprungs durch einen oft gänzlich verschiedenen Schwefelgehalt ausgezeichnet sind. Am Blutserum von Menschen, Rindern, Pferden, Schweinen und Hunden wurde der Schwefelgehalt derjenigen Globulinfraktion bestimmt, die durch 15–20-faches Verdünnen bei schwach essigsaurer Reaktion (Lacmus als Indicator) als Niederschlag erhalten werden konnte, und dann noch wiederholt aus verdünnter Lauge mittels Essigsäure umgefällt wurde. Es ergab sich aus diesen Bestimmungen, dass der Schwefelgehalt dieses Globulines nicht nur an verschiedenen Tierarten, sondern auch an verschiedenen Individuen derselben Tierart recht verschieden war, wie aus der kleinen Zusammenstellung weiter unten zu ersehen ist.

Dass diese Verschiedenheiten nicht durch methodische Fehler verursacht sind, konnte dadurch erwiesen werden, dass auch, wenn dasselbe Serum in Portionen parallel aufgearbeitet wurde, die Resultate in allen Portionen stets angenähert identisch waren. Und, dass diese Ergebnisse nicht ein Spiel des Zufalles darstellen, ging daraus hervor, dass der Schwefelgehalt des Fibrins, jedesmal mit dem Globulin derselben Tierart verglichen, parallele Schwankungen aufwies.

	GLOBULIN	FIBRIN
Mensch.....	1.17 (0.92–1.38)	
Rind.....	1.22 (1.16–1.28)	1.23 (1.20–1.23)
Pferd.....	1.10 (1.03–1.27)	1.18 (1.16–1.20)
Schwein.....	1.11 (0.99–1.30)	1.08 (1.07–1.09)
Hund.....	1.34 (1.15–1.60)	1.30 (1.24–1.42)

AUB, JOSEPH C., WALTER BAUER and FULLER ALBRIGHT (BOSTON).

The Influence of the Thyroid and Parathyroid Glands upon Inorganic Salt Metabolism.

Three individuals were studied:

1. A normal man who was given sufficiently large doses of parathyroid extract to raise the blood calcium level to 12.5 mgm. per 100 cc.
2. A myxedematous woman who was given enough thyroid extract to raise her basal metabolic rate to normal.
3. A woman with exophthalmic goiter who was cured by the surgical removal of her thyroid.

Calcium, phosphorus, and total base were determined in both urine and feces, and the urine excretion was analyzed for sulphur, chlorine, titratable acidity, nitrogen and ammonia.

These subjects received daily the same food, which was inadequate only in calcium. It is, therefore, easy to compare the effects of the varying conditions of the observation upon their inorganic salt metabolisms.

Daily injections of 100 units of Collip's parathormone raised the blood calcium level to 12.5 mgm. per 100 cc., lowered the blood phosphorus level, and increased the urinary calcium and phosphorus excretion. Thyroid administration markedly increased calcium excretion in the myxedematous case without affecting the blood calcium level. The exophthalmic goiter patient excreted 300 per cent more calcium than normal.

The effects of these internal secretion variations upon other factors of inorganic salt metabolism were surprisingly slight, and the variations that did occur were in large part due to changes in the nitrogen balance. Thus, the changes in fixed base metabolism are largely adjustments derived from the bone salts, but the other changes will also be described and discussed.

BABKIN, B. P. (MONTREAL). Innervation of the Salivary Glands.

Both the parasympathetic and sympathetic nervous systems supply the salivary glands with secretory fibres. Trophic (in Heidenhain's sense) influence is transferred to the glands through the parasympathetic nervous system. It is rather doubtful that the sympathetic nervous system has a trophic effect under normal conditions of activity of the glands. But the sympathetic nervous system sends motor fibres to the glands. Since the salivary glands and their ducts in the dog, cat and rabbit are completely deprived of muscular tissue, the contractility of the glands must be due to other elements (myo-epithelial cells, frame-work and diplosoma of the secretory cells, etc.), which may be looked on as contractile. The sympathetic motor fibres are paralysed by ergotamine. Histamine, which not only activates the salivary secretion but also presses out the saliva from the gland, is active after poisoning of the gland with ergotamine and atropine.

BACHEM, ALBERT and C. I. REED (CHICAGO). The Transmission of Ultra-Violet Waves by Live and Dead Tissue.

In previous reports it was shown that some of the effects of general cutaneous irradiation could be duplicated by direct irradiation of blood *in vivo* while others could not. This made it necessary to investigate quantitatively the transmission of spectral fields by skin. Comparisons on live and dead skin showed that for several hours after death skin preserved in Ringer solution behaved like live skin. If allowed to dry transmission was increased in the ultra-violet region. In live skin or preserved dead skin there was only 0.01 per cent transmission at 313 m μ and none at 302 m μ . The increased absorption toward the ultra-violet was due to true absorption which is a function of wave length while absorption due to scattering is practically constant.

BALDWIN, FRANCIS MARSH (LOS ANGELES). Simplified Digital Sphygmograph. (Demonstration)

Using the ordinary "Harvard" types of equipment for laboratory work in physiology, two adjustable iron stands mounting heavy muscle and a light heart lever respectfully are arranged in series. The long arm of the first lever is connected with the short arm of the second by a silk thread. By placing the end of the index finger under an appropriate finger pad of the first lever the heart-throb may be transmitted and amplified by the second lever so that a sphygmogram will result upon a properly adjusted drum. The usual features of a typical sphygmogram can be detected and analyzed, and because of the ease of assemblage and the comparative freedom from delicate adjustments the apparatus yields excellent results in the hands of the general student.

BALL, E. G. and D. WRIGHT WILSON (PHILADELPHIA). A Comparison of the Composition of Pancreatic Juice and of Blood Serum under Experimental Conditions.

Pancreatic juice was obtained by introducing a cannula into the major duct of the pancreas and collecting portions of juice after injecting secretin. The secretin was prepared by the very convenient method of Cowgill and Mendel.¹ Analyses of pancreatic juice and blood serum obtained at about the same time showed that the sodium concentration was slightly higher in the juice than in the serum; the potassium concentration was about the same in both; and the calcium, magnesium and phosphate concentrations were much lower in the pancreatic juice. The sum of the basic ions was somewhat higher in the juice than in the serum. The chloride and bicarbonate varied considerably and varied inversely so that the sum of the two was rather constant. The pH of the pancreatic juice is apparently regulated by the secretion of a constant concentration of base and varying concentrations of chloride. During rapid secretion after secretin the chloride is about half the bicarbonate while juices slowly secreted may contain a chloride concentration five times that of the bicarbonate. These two ions make up almost the total acid radicals in pancreatic juice. Juices which are secreted slowly are less alkaline and contain higher concentrations of calcium, magnesium and phosphate.

The permeability of the membranes to salts injected into the blood stream was studied by obtaining portions of pancreatic juice by repeated injections of secretin before and after the injection of salt solutions. After the injection of hypertonic sodium chloride intravenously the concentrations of sodium in serum and pancreatic juice rose equally. A similar result was obtained with potassium. After calcium, magnesium and phosphate injections the concentrations of these ions rose in pancreatic juice but remained far below the concentration in serum. The pH and bicarbonate concentration of pancreatic juice seem little influenced by injections of acid and alkali.

BALLS, A. K. and E. WALDSCHMIDT-LEITZ (PRAGUE). Concerning Animal Dipeptidase and Polypeptidase.

Important resemblances between the proteases of animal and plant origin have recently been pointed out, while the corresponding peptid splitting enzyme systems appeared to be quite different. It is now shown that the so-called "erepsin" of the animal intestinal tract and many animal tissues, is a mixture of two independently acting enzymes, a polypeptidase and a dipeptidase, whose behaviour resembles that of the corresponding plant enzymes.

The polypeptidase and dipeptidase in erepsin may be separated by ferric hydroxide, which completely adsorbs the dipeptidase from acid solutions, leaving the polypeptidase almost quantitatively unadsorbed. By elution of the adsorbate with ammonia, the dipeptidase is obtained and contains only traces of the polypeptide splitting enzyme.

The splitting of tri-peptides such as leucyl-glycyl-glycine is a monomolecular reaction. Within wide limits, the reaction constant is proportional to the amounts of enzyme present, permitting their accurate quantitative estimation.

¹ Cowgill, G. R. and L. B. Mendel. Amer. Journ. Physiol., 1921-22, lviii, 131.

The two enzymes are absolutely distinct in their behaviour toward different substrates. The polypeptidase splits tri, tetra, penta, and hexa peptides composed of leucine and glycine residues, and in all probability would split the still higher members of these series. For the action of the polypeptidase a free amino group is required in the substrate, and also the farther condition that the peptid linkage attacked shall not be adjacent to a free carboxyl group. The dipeptidase, on the contrary, is able to attack a peptid linkage adjacent to a free carboxyl group. The dipeptidase also requires a free amino group, but not a free carboxyl group, as does the plant dipeptidase. In this respect the animal and plant dipeptidases are distinguishable.

The separate, yet side by side existence of a dipeptidase and a polypeptidase in the intestine, may well have a bearing upon the question of the extent to which ingested proteins are broken down before the products of digestion become absorbable from the intestine.

BARBOUR, H. G., B. E. RUSSELL, S. H. FLOWERS, E. S. DUNHAM and L. G. HUNTER (LOUISVILLE). **The Significant Redistribution of Water Between Internal and Surface Tissues and the Blood at the Height of Morphine Withdrawal.**

Well advanced morphine addiction in dogs (daily dose, 30 mgm. per kilo) tends to dehydrate certain internal organs, viz.: liver, kidney, brain. Conversely the surface tissues (skin (?), stomach, intestine) and blood (whole blood, serum, spleen) tend to show hydration. Environmental exchange (volume of water ingested and of urine) is always low at first, but may increase later.

Remarkable redistribution of water occurs upon sudden withdrawal from morphine. The effects are most pronounced during the first days, accompanying the characteristic muscle tremors and diarrhea.

Internally, edema of the brain (with lipid loss in some parts) and of muscles, liver and kidney occurs. The heart muscle remains constant but the pericardial fluid increases.

Blood, serum, spleen and surface tissues all, on the other hand, show a considerable loss.

The environmental water exchange is greatly increased. When the latter subsided early, the withdrawal edema also ceased, the dehydrated surface tissues and blood remaining dry. When, however, the high environmental exchange continued, the blood soon began to show hydration.

Of a litter of five females, five months old, four were addicted; three of these ate throughout the same balanced Cowgill synthetic ration as the control unmorphinized dog; two dogs were withdrawn after five weeks. All were killed quickly with KCN. In other dogs internal tissues were repeatedly sampled under local anesthesia.

The results appear unrelated to nutrition. Ingestion was constant; nitrogen absorption was nearly complete under both addiction and withdrawal.

Confirmatory results in rats included on withdrawal, liver and brain hydration, anhydremia and dehydration of skin. Addicted rats differed from dogs by *increasing* their environmental water exchange, which on withdrawal fell suddenly as did body weight and temperature, later in withdrawal water exchange became supernormal.

Like *tetany* morphine withdrawal shows: muscle tremors, incoördina-

tion, decreased blood calcium, edema of brain, liver and kidneys, anhydremia, diarrhea and disturbed temperature regulation. Especially significant is a degree of brain edema which should in man suffice to produce psychic symptoms.

BARBOUR, H. G., B. E. RUSSELL, S. H. FLOWERS, E. S. DUNHAM and L. G. HUNTER (LOUISVILLE). Muscular Effects Suggesting Tetany at the Height of Morphine Withdrawal. (Cinematograph demonstration)

BARKAN, GEORG (FRANKFURT A. M.—DÖRPAT). Zur Differenzierung biologischer Eisenverbindungen.

Ausser dem Blutfarbstoff (Hb) und seinem direkten Abkömmling, dem Hämatin, wurden in letzter Zeit einige eisenhaltige Verbindungen des tierischen Organismus von verschiedenen Autoren eingehender untersucht. Sowohl das eisenhaltige "Atmungsferment" (Fe), wie O. Warburg nachwies, als auch jener Teil des "leicht abspaltbaren" Bluteisens (Barkan), dessen Ionisierung mittels verdünnter Säure, wie Barkan und Berger zeigten, durch CO oder Austreiben des dissoziablen Sauerstoffs vollständig gehemmt wird (E), reagieren nach ähnlichen Gesetzmässigkeiten wie der Blutfarbstoff mit CO und O₂. Hinsichtlich der Verteilung von Hb, Fe und E zwischen jenen beiden Gasen ist wichtig, dass die relative CO-Affinität am kleinsten bei Fe, am grössten bei E ist. Ein kleinerer Teil des "leicht abspaltbaren" Bluteisens (E'), zu dem auch das Plasmaeisen gehört, scheint nicht mit CO und O₂ zu reagieren. Auch für das Cytochrom (Keilin), jenes in tierischen und pflanzlichen Zellen weit verbreitete eisenhaltige Pigment, scheint erwiesen, dass es nicht mit CO reagiert, während es mit O₂ eine leicht reduzierbare Verbindung bildet. Fasst man mit Warburg die Katalase als ein ebenfalls eisenhaltiges Ferment auf, so fällt hinsichtlich der Katalase des Blutes eine mehrfache Analogie ihrer Eigenschaften zu solchen des "leicht abspaltbaren" Bluteisens in die Augen. Wie das "leicht abspaltbare" Eisen ist auch die Katalase im wesentlichen an die Formelemente des Blutes gebunden, mit dem Blutfarbstoff vergesellschaftet, ohne zu ihm zu gehören und in quantitativer Hinsicht von der Menge des Hb unabhängig. Prüft man das Verhalten der Blutkatalase gegenüber CO, so zeigt sich ihre Wirkung ganz im Gegensatz zum Verhalten des abspaltbaren Eisens, wenigstens bei Atmosphärendruck, unabhängig von der Gegenwart des CO. Hieraus darf man schliessen, dass die Blutkatalase nicht mit E identisch ist. Gegen eine Identität mit E' wiederum, jenem durch CO nicht hemmbaren Teil des "leicht abspaltbaren" Eisens, spricht die Tatsache, dass Blausäure die Katalasewirkung hemmt, dagegen weder mit E noch mit E' zu reagieren scheint.

BARLOW, O. W. (CLEVELAND). A Comparison of Bicarbonate and Phosphate Buffers and CO₂ on the Function of the Perfused Frog Heart.

The multiplicity of "Ringer's" solutions which have been and are being used by various authors for perfusion purposes and which vary as to ionic content, pH, buffering agents and CO₂ content suggested a study of the reactions of the perfused frog heart to one of the relatively standard solutions such as the Howell-Ringer solution (consisting of 0.7 per cent NaCl, 0.025 per cent anhyd. CaCl₂, and 0.03 per cent KCl) with the bicarbonate or phosphate buffers, calcium content, O₂ and CO₂ mixtures or CO₂ for aeration purposes and alteration of the pH as variables, in order

to determine the optimal solution for frog heart perfusions. The addition of 0.1 per cent glucose to the Howell solution was found to prolong the period of optimum reactions.

The substitution of a bicarbonate buffered Ringer's solution (with concentrations of bicarbonate ranging from 0.008 to 0.12 per cent and pH 7.2) during a 20 to 30 minute perfusion for a NaOH Ringer of similar pH (both solutions being aerated with O_2) resulted either in a slight depression of the rate, excursions and both systolic and diastolic tone or practically no demonstrable change. The maximal, median alteration observed varied from a 5 per cent increase in excursions to a $9\frac{1}{2}$ per cent decrease in rate. Increasing the alkalinity from a normal level (7.2) to a pH of 8.0 apparently increased the susceptibility of the heart to the depressant effects of bicarbonate since subsequent substitution of NaOH Ringer's solution for the bicarbonate was usually followed by recovery.

The use of NaOH for correcting the pH of perfusion solutions resulted in a solution optimal for the frog heart. During a 2 to 3 hour period however (room air being used for aeration), the pH may fall as much as 0.4 of a point. A bicarbonate buffered perfusate (which maintains a constant pH level under similar aeration conditions) would consequently be preferable for experiments where successive perfusions under standard conditions are required.

The substitution of a fresh Na_2HPO_4 buffered Ringer's solution for a bicarbonate Ringer's solution of the same pH results during a 20 minute perfusion in an improved inotrope, a median improvement in tone and a slightly diminished chronotrope, with concentrations of phosphate ranging from 0.008 to 0.024 per cent inclusive. Higher concentrations of phosphate depress the rate, excursions and tone, the extent of which may vary from 10 per cent with 0.048 to 100 per cent with 0.096 per cent within 5 minutes. These depressive functional changes are due in part to alterations of pH (changes which increase in proportion to the phosphate concentration and the age of the solution), partly to precipitation of the calcium ions, and with high concentrations of Na_2HPO_4 to the phosphate ion *per se*.

The perfusions of bicarbonate buffered Ringer's solution (pH 8.0) aerated with 95 per cent O_2 and 5 per cent CO_2 or with pure CO_2 produced changes which were directly associated with alterations of pH. Over a short range, cardiac function improved as the alkalinity decreased toward neutrality. Beyond this optimal range however, cardiac function diminished progressively. These effects may be duplicated either on the same or different hearts by perfusing the same but CO_2 free perfusates the pH of which have been corrected to the same degree with HCl.

The perfusion of a solution (pH 7.2) buffered with bicarbonate and containing 0.0187 per cent $CaCl_2$ ($\frac{3}{4}$ normal concentration) did not produce any significant alteration of the cardiac function. After 25 minutes the median maximal change did not exceed $-2\frac{1}{2}$ per cent. Further reduction of the calcium content of the perfusate (other factors remaining constant) definitely diminished the mean cardiac activity as to rate, amplitude and especially auricular tone. With $\frac{1}{2}$ and even temporarily with $\frac{1}{4}$ the normal calcium content the rate may be improved slightly but the diminished inotrope more than compensates for the small chronotropic improvement. With subnormal concentrations of calcium, the height of the excursions was depressed primarily and the rhythm secondarily. The magnitude

of these changes was almost directly proportional to the extent of calcium reduction.

BAUDISCH, OSKAR (NEW YORK UND STOCKHOLM). Röntgenographische und magnetometrische Methoden zur Erforschung der Chemie der Grenzflächen. I. Über raumisomere Eisenoxyde und Eisenoxyhydrate.

Die Versuche wurden mit einfachen Eisenoxyden und Eisenoxyhydraten, die alle aus reinstem Eisen (aus Eisencarbonyl) hergestellt waren, ausgeführt. Die chemische Charakteristik dieser raumisomeren Eisenverbindungen wurde durch katalytische Oberflächenreaktionen (Katalase, Benzidinoxydation u.a.m.) geprüft, während ihre biologische Aktivität durch den Einfluss auf den Stoffwechsel gewisser Bakterien untersucht wurde. Nach Aufnahme von Röntgenogrammen bekam man Aufschluss über die Atomarchitektur (Feinstruktur) und über die Teilchengröße dieser Stoffe. Um ferner auch den subtilen Unterschieden ihrer Oberfläche und den Spannungserscheinungen in den Mikrobausteinen (Feinstruktur) nachzuspüren, wurden magnetometrische Messungen ausgeführt.

BAUDOUIN, A. ET J. LEWIN (PARIS). Le dosage de la matière réductrice du sang et la nature des sucres du sang.

I. Les auteurs présentent une nouvelle méthode de dosage du sucre du sang qu'ils emploient depuis 3 ans avec toute satisfaction. Elle consiste essentiellement: a) à désalbuminer le sang au moyen d'une solution nitro-mercurielle; b) à pratiquer le dosage par réduction d'une liqueur du type SACHSSE, à base d'iodo-mercure de soude; c) à doser le mercure précipité au moyen d'une méthode à l'iode. On ajoute de l'iode en excès. Une partie transforme le Hg en $Hg I_2$ et disparaît. Le reste est dosé par l'hyposulfite.

Pour les détails de la technique voir: A. Baudouin et J. Lewin: Bulletin Soc. Chimie Biol. Tome IX No. 3, Mars 1927 et A. Baudouin ibid. Tome X No. 8 Sept-Oct. 1928.

II. Cette méthode peut s'appliquer à des quantités de sang allant de 0,2 cm³ à 1 cm³. Elle présente des avantages au double point de vue pratique et théorique.

a. le Hg produit ne présente aucune tendance à l'oxydation, au contraire de l'oxyde cuivreux.

b. La méthode est très régulière et très rapide. La réduction des liqueurs mercurielles se fait très vite. Un dosage ne demande, en tout, pas plus d'une dizaine de minutes.

c. La réduction est, dans de larges limites, indépendante de la concentration, de l'alcalinité, du temps de chauffage. Les conditions sont bien moins étroites que pour les méthodes au cuivre.

III. Les résultats fournis par cette méthode, oscillent, pour le sang normal, autour de 0 gr. 80 de sucre, estimé en glucose. Ils sont donc du même ordre que ceux que l'on obtient par les méthodes Américaines les plus récentes. Le glucose ajouté au sang est retrouvé avec une bonne approximation.

Les auteurs pensent que leur méthode dose essentiellement le glucose du sang. Ils estiment néanmoins qu'il est impossible de l'affirmer et que le dernier mot est loin d'être dit sur la nature des sucres du sang. Il serait d'un haut intérêt de posséder une méthode de dosage spécifique de

glucose. Ils ont pu adapter la méthode biochimique de Bourquelot au dosage spécifique de minimes quantités de glucose, mais l'application de ce procédé au sucre sanguin n'est pas encore achevée.

BAUMBERGER, J. PERCY, R. T. BIGOTTI and KATHLEEN BARDWELL (PALO ALTO, CALIFORNIA). **The Photodynamic Action of Methylene Blue on the Clotting Process.**

The coagulation of plasma may be completely inhibited by the photodynamic action of methylene blue. The anticoagulant property of methylene blue has been noted by Lefrou without mentioning the action of light and Howell has described a similar photodynamic action of eosin and hematoporphyrin without reference to oxidation.

A fibrinogen solution which clots in three minutes after the addition of calcium and prothrombin can be completely inhibited if one part in ten thousand of methylene blue is added and the mixture immediately exposed to visible light of wave lengths absorbable by the dye. If not exposed to light the coagulation will take place normally. Oxygen is necessary to the action of the dye as complete evacuation will prevent the photodynamic action. Certain readily oxidizable compounds, resorcin, casein and tyrosine will protect the clotting system as in the eosin hemolysis described by Schmidt and Norman.

Quinhydrone, indophenol and ferricyanide will not permit the photodynamic action of methylene blue in the absence of oxygen. The reducing action of light on methylene blue in the presence of organic matter (Perret) may be through accompanying peroxide formation, the oxidative mechanism inhibiting the clotting process. However, cyanide, peroxide or ZnO do not influence the effective time of exposure. Oxygen is consumed and CO₂ liberated during the photolytic process.

BAYLISS, L. E. (LONDON), B. FREEMAN, A. E. LIVINGSTON, A. N. RICHARDS and A. M. WALKER (PHILADELPHIA). **Further Quantitative Studies of the Composition of Glomerular Urine from Frogs' Kidneys.**

In a series of estimations of the chloride concentration of frogs' glomerular urine, evidence has been obtained which only to a limited degree confirms that previously published by Wearn and Richards, namely, that the chloride concentration of glomerular urine is higher than that of the plasma from which it is derived. In 19 experiments the frog's kidney was perfused with modified Ringer's fluid (oxygenated); in 17 of these glomerular chloride differed from plasma chloride by only 10 per cent or less. Twenty experiments were made on living frogs; in 11 the chloride figures for glomerular urine and plasma agreed; in 9 the former was higher by from 13 to 100 per cent. In all of these experiments the tubule was open during the glomerular collection which was made with negative pressure.

Quantitative comparisons of glomerular fluid and plasma have been made with respect to elimination of phenol red and indigo carmine. When the neck of the tubule was closed during glomerular collection, the concentration of dye in the glomerular fluid was less than that in the plasma by a difference equivalent to that between plasma and an ultrafiltrate from it.

Barger's method for estimating molecular concentration, applied in 40 experiments, showed that the molecular concentration of frog's glomerular urine was consistently the same as that of the plasma within the limits

of error of the methods. In these experiments the tubule was closed during the collection and collection was made against positive pressure.

A means for estimating electrical conductivity in very minute amounts of fluid was developed. In the 6 experiments which were most nearly perfect technically the figures for electrical conductivity of glomerular fluid and plasma agreed within 10 per cent or less.

We conclude that the best quantitative evidence at present available from frogs is in harmony with the filtration hypothesis of glomerular function. It appears that the neck of the tubule should be closed when glomerular fluid is being collected.

BAZETT, H. C. and B. MCGLONE (PHILADELPHIA). A Chemical Factor in the Stimulation of Nerves Giving Temperature Sensations.

Temperature changes in the tissues have been recorded. The results often fail to confirm current hypotheses. Thermocouples of fine wire (McGlone loop type) are placed in the dermis. The second couple is located on the surface immediately above its fellow, constituting a "differential," directly measuring gradients. Surface temperatures are recorded by loop couples of the usual type. The rectal temperature and that of a bath are recorded by resistance thermometers. The hand and forearm are immersed in rapidly stirred water. After long immersion in a bath at rectal temperature stasis is maintained for five minutes. On release a sensation of warmth appears within two seconds and lasts $\frac{1}{2}$ minute. There is no change of temperature; the gradients are throughout slight and in either direction.

Within a bath at 40.0° continued sensations of warmth ensue after establishment of equilibrium, with a reversed gradient. The gradients diminish during stasis, are slowly reestablished on release. Slight warmth may be noted towards the end of stasis, intense warmth $1\frac{1}{2}$ seconds after release continuing more than 50 seconds. One hour immersion in a bath at 26° followed by compression and release may give a rise of temperature at 2.0 mm. depth of 2.2° in 20 seconds without thermal sensation.

Following stasis, sensations are not correlated with observed thermal gradients (though they appear to be related under other conditions), but closely parallel acid changes in the skin. The sensations arise when a wave of blood of increased acidity (probably previously stagnated in the muscles) passes through the skin. A temperature rise also produces an increase in acidity in the tissues *in vivo* as in blood *in vitro*; so it is possible that acid-base gradients arise from temperature gradients and are the direct stimuli. Following stasis an acid-base gradient, whether of metabolic or thermal origin, may act as the stimulus. The differences in the character of the sensations induced in the muscular forearm and non-muscular finger would be thus explained, as well as the absence of sensations when the alkalinity of cold is balanced by the acidity of stasis.

BELLIDO, J. M. (BARCELONA). De la réaction actuelle de l'urine sécrétée par les reins privés de leur innervation.

Comme je l'ai montré avec Puche en 1924 (Comptes-rendus de la Soc. de Biologie de Paris, xc, 827), l'urine des reins dénervés a perdu les relations de dépendance avec les variations de la teneur en ions hydrogène du sang et des tissus, qui caractérisent l'urine sécrétée par les reins ayant conservé leurs nerfs. De nos expériences on doit déduire que les reins

privés de leur innervation, pendant les 10-12 jours suivant l'opération, réagissent plus lentement que les reins normaux, et, passé le 12^{me} jour, réagissent plus vite. D'autre part, l'urine des reins dénervés présente rarement à la suite d'une injection d'acide dans le sang, un pH aussi bas que celui de l'urine sécrétée par des reins non dénervés. Mes expériences les plus récentes, faites en collaboration avec Fernandez Riofrio, confirment en tous points les résultats obtenus en 1924.

BELLUCCI, L. (SIENA). Ricerche sulla permeabilità intestinale nell'insufficienza paratiroidea sperimentale.

L'A. continuando le ricerche già iniziate dallo Spadolini sulla permeabilità intestinale negli animali paratiroidoprivi ha trovato particolarmente interessante il comportamento dell'intestino di fronte all'assorbimento della colina. Sono stati particolarmente studiati gli stadi più precoci della disfunzione paratiroidea, quando cioè è meno facile rendersi chiaro conto delle condizioni abnormi della mucosa intestinale.

Le anomalie dell'assorbimento intestinale sono state messe in evidenza indagando il comportamento della pressione sanguigna e del ritmo cardiaco in seguito ad una iniezione diretta di colina nel tenue, in dosi tali da rimanere assolutamente prive di effetti in animali normali.

Nell'insufficienza paratiroidea si è potuto così constatare la grande facilità con cui la colina penetra in circolo, confermando l'esperimento quelle abnormi condizioni di permeabilità intestinale (particolarmente evidenti rispetto a sostanze a tipo di amina) che secondo lo Spadolini hanno parte notevolissima, in concomitanza dello stato ipocalcemico, nel determinismo della sindrome paratiroidopriva.

BELLUCCI, L. (SIENA). Sulla nuova sede del centro corticale laringeo nel cane.

L'A. con una serie di lavori eseguiti allo scopo di una più esatta localizzazione del centro corticale laringeo ha potuto mettere in evidenza i seguenti fatti:

1°. Nel cane il centro corticale laringeo è situato non già nella sede stabilita da Krause ma nella seconda circonvoluzione cerebrale (gyrus coronalis) al davanti del centro per l'arbitolare delle palpebre, nella regione della faccia analogamente a quanto egli stesso ed altri autori hanno osservato nelle scimmie.

2°. In detto centro sono rappresentati, e fino ad un certo punto differenziabili, un centro per l'adduzione delle corde vocali, un centro per l'elevazione del laringe ed uno per l'abduzione delle corde vocali. Quest'ultimo è più difficilmente rilevabile data la sua associazione funzionale col centro bulbare respiratorio. Nel suo insieme il centro corticale laringeo costituisce un focolaio complesso da cui originano gli impulsi superiori per movimenti coordinati dell'organo. Prossimo ad esso è il centro per i movimenti della lingua.

3°. Con adatte stimolazioni ed in speciali condizioni è possibile ottenere una dissociazione tra i movimenti fonatori laringei e i movimenti respiratori toracici.

4°. La distruzione di questo centro come pure quella del centro di Krause non determinano gravi modificazioni nell'emissione di suoni; colla prima però si manifestano fenomeni di deficienza funzionale nei muscoli e nella sensibilità della faccia, colla seconda nei muscoli della nuca.

5°. La rappresentazione corticale è bilaterale, simmetrica, a funzione pressochè sinergica sulle due corde vocali.

6°. Il metodo delle degenerazioni discendenti rivela alterazioni localizzate nelle vie piramidali, nella capsula interna in corrispondenza del ginocchio e del suo estremo posteriore, nel bulbo in corrispondenza della superficie antero interna.

7°. Il metodo delle atrofie e delle sclerosi rivela alterazioni nel nucleo bulbare del vago nonchè nella 2ª circolazione corticale con la scomparsa iniqua delle grandi cellule piramidali nella zona corrispondente alla particolare sede messa in evidenza col metodo della stimolazione diretta.

BELOUSSOFF, N. (CHARKOFF). The Elasticity of Muscle.

The method of experimentation: The elongations are observed with a graphic method (curves are obtained) and with a cathetometer (marks on the muscle itself); the loading discontinuous and continuous.

Results: Elongations are not proportional to the weight, irregular in each case on the loading with small and more considerable weights equally, but here the irregularity is more conspicuous.

The curves of extensibility in various and even in the same conditions are not uniform but very complicated. Experiments are made with a tendon and a piece of rubber band, with anaesthetised (morphin, cocain) and curarised muscle; now elongations are regular and uniform.

BENNATI, D. et J. CUZIN (PARIS). La reserve alcaline après excitation du bout périphérique du splanchnique.

Sur le conseil de M. J. Gautrelet et comme suite à la note qu'il publie à ce Congrès avec ses Collaborateurs, nous avons recherché quelle était l'action de l'excitation du bout périphérique du splanchnique sectionné sur la respiration et la reserve alcaline.

D'accord avec Gley et Ozorio de Almeida d'une part, Tournade de l'autre, nous n'avons pas observé d'apnée, mais une diminution nette de l'amplitude et du nombre des mouvements respiratoires. Quant à la reserve alcaline, nous avons constaté chaque fois une hausse manifeste, que l'excitation à l'écue d'un courant induit de 20 microcoulombs fut prolongée 2 et 3 minutes ou courte au contraire de 20 à 30 secondes.

C'est ainsi qu'elle passa (expérience 1451) après 3 minutes d'excitation de 55 à 66 et (expérience 1453) après 30 secondes de excitation, de 57 à 67.

Cette hausse de la reserve alcaline apparait environ 2 à 3 minutes après le debut de l'excitation du splanchnique.

Deux minutes plus tard on constate déjà un chiffre de la reserve alcaline égal à la normale.

La pression enregistrée traduisait, après une phase de vasoconstriction une periode de ralentissement du coeur, avec augmentation de son amplitude, caracteristique de la secretion adrenergique.

Nous avons lié, en maniere de contre epreuve, les veines de la surrenale dont le splanchnique était excité, et dans ces conditions il n'est apparu aucune modification de la reserve alcaline, seule d'ailleurs était observée une phase de vasoconstriction. Aucun effet respiratoire n'était enregistré.

BERG, CLARENCE P., WILLIAM C. ROSE, AND CARL S. MARVEL (URBANA).

The Biological Substitution of Synthetic Compounds in Place of Tryptophane for Purposes of Growth.

Synthetic compounds more or less closely related to tryptophane have been fed to rats upon tryptophane-deficient diets in order to determine whether the substances in question are capable of serving in place of the amino acid for purposes of growth. The compounds employed were of two general classes, namely: 1, those derived from tryptophane by the introduction of substituent groups in one of the functional positions of the amino acid, and 2, those which were synthesized from simpler compounds and contained no amino group at all.

Studies involving the first class of compounds have shown that methylene-tryptophane and benzoyltryptophane are unable to support the growth of rats upon tryptophane-deficient rations. The introduction of the $\text{CH}_2 =$ or $\text{C}_6\text{H}_5 \cdot \text{CO}-$ radical in place of hydrogen in the amino group renders the resulting product utterly useless from the nutritive standpoint. On the other hand, acetyltryptophane and tryptophane ethyl ester hydrochloride are utilized for growth purposes just as satisfactorily as is free tryptophane. In the case of the ethyl ester hydrochloride it is quite possible that the free amino acid may be liberated in the alimentary tract. Indeed, experiments *in vitro* showed that esterases readily accomplish this hydrolysis. With acetyltryptophane, however, evidence of *alimentary* deacetylation is not so easily secured. Extracts of the intestinal mucosa of rats, as well as solutions of commercial enzymes, liberate the amino acid from the derivative *very slowly*. Inasmuch as the compound promotes growth as satisfactorily as does the free amino acid, it appears likely that deacetylation occurs largely after absorption from the intestine. If this be true, the experiments afford an illustration of a reversal of the reaction of biological acetylation observed by Knoop and Kertess¹ and others.

In the experiments involving the replacement of tryptophane by compounds of the second class, the results indicate that indole propionic acid is incapable of serving in place of the amino acid. On the other hand, *indole pyruvic acid induces a rapid growth in animals upon tryptophane-deficient diets*. In a former communication² from this laboratory it was shown that dietary histidine may be replaced by imidazole lactic acid. Harrow and Sherwin³ report that a similar substitution may be accomplished by the use of imidazole pyruvic acid. The results of the present investigation are of interest as illustrating the replacement of a *second* "indispensable" amino acid of the diet by a synthetic non-amino compound.

BERITOFF, J. (TIFLIS). **On the Conduction Time of the Nervous Impulses Through the Central Nervous System.**

We investigated the conduction time of the nervous impulses through the central nervous system of cats in normal condition and after strychnine poisoning. For this purpose we stimulated the afferent nerve or the skin of one of the limbs and registered action currents of the muscle with a string galvanometer.

¹ Knoop, F. and E. Kertess. *Zeitschr. physiol. Chem.*, 1911, lxxi, 252.

² Cox, G. J. and W. C. Rose. *Journ. Biol. Chem.*, 1926, lxxviii, 781.

³ Harrow, B. and C. P. Sherwin. *Journ. Biol. Chem.*, 1926, lxx, 683.

1. The rhythm of stimulation of the afferent nerve (10-20 per second) is transferred through the spinal cord to the muscles of the stimulated limb in ipsilateral flexor reflexes. If a reflex occurs in other limbs, it is impossible to notice the rhythm of stimulation in the action currents of the muscles, excluding a few exceptional cases.

2. The minimal latent period of the muscles' electrical responses which arise following the rhythm of stimulation corresponds, very often, exactly to the length of the nervous path from the stimulated nerve to the spinal cord and back to the muscle. The rate of conduction of nervous impulses is considered to be equal to 70-80 meters per second and the latent period of the electrical response of the muscle stimulated indirectly is equal to 0.0015 second. Therefore, the excitatory processes may spread through the short reflex arcs without delay.

3. After general strychnine poisoning the rhythm of stimulation is transferred before the spasms also to the muscles of the contralateral side. The latent period of electrical response of the ipsilateral muscle is the same as in the normal animal. The latent period of the muscles of the opposite homonymous limb is identical with the latent period of the stimulated limb. Therefore, excitatory processes are transferred without delay from one symmetrical half of the spinal cord to another.

4. At the stage of strychnine spasms as well as slightly before it, the stimulation evokes reflex reactions of the entire muscular system and sometimes the action currents follow exactly the stimulation rhythm. The electrical responses during these reactions occur a little later as compared with the above mentioned ipsilateral electrical effects. There exist certain indications as to the occurrence of these common effects through the cerebral cortex, *viz.*, their conduction time corresponds exactly to the length of the nervous paths going from the stimulated nerve to the cortex and back to the registered muscle. This conduction time is often prolonged 2-3 σ and this additional time falls in the cerebrum. Therefore, through the entire nervous system and in certain cases in the cerebrum itself, the excitatory process is spread almost without delay.

5. Several experiments on the stimulation of the motor cortex have been made in order to study the conduction time from the cortex to the muscles. It appeared that in certain conditions this time corresponds exactly to the length of the nervous path and in other conditions is by 1-2 σ longer before strychnine poisoning as well as after it.

6. On the basis of these experiments it is suggested that, in the same manner as in the nerve fibre, the passage of excitatory processes from the excited part to the non-excited part may depend upon the stimulating action of electrical effects of the former upon the latter (Hermann, Cremer). The passage of excitation from one neurone to another may be conditioned by the stimulating action of the electrical response of nerve endings of one neurone on the cell body of another neurone.

BERITOFF, J. (TIFLIS). Excitation of the N. Ischiadicus of a Frog by Action Currents of the Thigh Muscles without Altering their Normal Disposition in the Leg. (Demonstration)

BERTRAND, IVAN et L. JUSTIN-BESANÇON (PARIS). Utilisation de la lumière infra-rouge pour l'étude histo-physiologique du tube contourné du rein.

Trois principes sont à la base de la technique employée par les auteurs:

- 1° L'utilisation d'une lumière de très grande longueur d'onde, assez peu réfrangible pour n'être pas arrêtée par les fins colloïdes du cytoplasme.
- 2° L'emploi comme colorant histologique de sensibilisateurs photographiques (cryptocyanines), de sorte que les zones d'absorption de la coupe correspondent aux zones de sensibilisation de la plaque photographique.
- 3° La sensibilisation de l'émulsion photographique aux infra-rouges et l'élimination par un écran de tout le spectre visible.

Cette méthode permet d'obtenir des photogrammes parfaitement nets aux plus forts grossissements. Son application à l'étude du tube contourné dans la série animale révèle des détails intéressants sur: a) La structure de la bordure en brosse et les connexions de ses éléments avec le cytoplasme. b) L'existence d'un appareil granuleux, dont les éléments apparaissent sur tous les photogrammes en infra-rouge, alors qu'ils manquent complètement à l'examen microscopique visuel; les auteurs discutent les rapports de cet appareil granuleux avec le chondriome et le vacuome. c) Des détails de structure du noyau et des séparations intercellulaires.

Au point de vue physiologique, une diurèse légère détermine l'apparition d'innombrables plastas opaques aux infra-rouges. Une diurèse plus abondante amène une vacuolisation du cytoplasme. L'acidose entraîne l'imperméabilité des noyaux aux infra-rouges. Dans les étapes initiales de l'intoxication par le nitrate d'urane, des plastas, semblables à ceux qui marquent la diurèse, apparaissent dans le cytoplasme. L'anastomose urétéro-veineuse bilatérale amène le déplacement des noyaux vers la membrane basale et l'accumulation des éléments granuleux dans la zone apicale. La mort provoque la coalescence des éléments de l'appareil granuleux. La préparation d'un colorant vital qui serait en même temps un sensibilisateur photographique en infra-rouge permettrait de préciser de nombreux points de la physiologie du cytoplasme.

BEST, C. H. and E. W. McHENRY (TORONTO). The Inactivation of Histamine.

This paper reports the results of further work on the *in vitro* inactivation of naturally occurring and added histamine by lung tissue. The new experiments deal with the optimum temperature and hydrogen-ion concentration of the action of the factor present in minced lung. Various tissues from different animals have been studied to determine the distribution of this histamine-inactivating property in the animal body. The preparation and purification of extracts containing the active factor are discussed.

BETHE, A. (FRANKFURT A. M.). Über die Permeabilität der Körperoberflächen von Seetieren.

Die von Frédéricq und Bottazzi aufgestellte und gut begründete Lehre von der Semipermeabilität der Körperoberflächen von Seetieren lässt sich nach Untersuchungen mit neueren Methoden nicht mehr aufrecht erhal-

ten. Sowohl Anionen wie Kationen, besonders diejenigen, die im normalen Seewasser enthalten sind, können durch die Körperoberfläche hindurchtreten. Die Geschwindigkeit, mit der dies geschieht, ist je nach der Tierart verschieden. Hieraus erklärt sich die verschieden grosse Empfindlichkeit, welche die Seetiere gegenüber Veränderungen in der Zusammensetzung des Seewassers zeigen.

BEUTNER, R. (LOUISVILLE). **The Source of Bioelectricity, Investigated by Means of the Relation Between Stainability and Electric Charges in Tissues and Artificial Models.**

1. Numerous experiments have demonstrated the following relation between the stainability of tissues and bioelectric currents: structures bearing a relatively negative charge are preferably stained by *eosin* and certain other acid dyes, while electrically *positive* structures seem to attract *methylene blue* and other staining bases; as expressed by the following scheme:

- saline soln.	acidophilic structure stained by eosin	basophilic structure stained by methylene blue	saline soln. +
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E.g., G. W. Crile¹ found a parallelism between the current intensity and staining intensity of tissue, also many other observations which tend to support this view, (to be discussed later). R. Keller,² R. Fürth,² J. Gicklhorn² *et al.* have offered definite experimental proofs for the above relation by studying the stainability and electromotive forces of plant tissues.

2. Artificial systems have now been found which exhibit the same relation between stainability and electromotive forces; one such system is the following cell:

+ saline soln.	layer of olive oil + oleic acid (with or without amine) (basophilic) I	layer of olive oil + amylamine (acidophilic) II	saline - soln.
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When shaken with a mixture of methylene blue and eosin (Wright's stain), *I* stains like acidophilic, *II* like basophilic tissue.

The technical difficulty of measuring the electromotive force of such a cell system, in spite of its enormous resistance, was overcome by special methods.

3. The apparent similarity of these systems to tissues *does not* prove that fats are the cause of bioelectricity. Proteins might be used in the place of fats if the present technical difficulties can be overcome.

In general, many *water immiscible* phases with basic (or "acidophilic") properties will be electrically positive against *water immiscible* phases with acid (or "basophilic") properties.

¹ G. W. Crile. Arch. Surg., 1921, 25, and numerous other publications.

² R. Keller, "Elektric. in der Zelle," II ed., Prag, 1925.

R. Fürth, Naturwissenschaften, 1928, xvi, 777.

J. Gicklhorn and K. Umrath. Protoplasma, 1928, vi, 228.

4. The *water immiscibility* of the acid or the base used is essential. If the differential stainability of the two phases is chiefly produced by adding water soluble acids or bases—thus altering the pH—the *opposite effect* on both stainability and electromotive forces is found. E.g., in Loeb's¹ gelatin systems:

— saline soln.	acidophilic gelatin chloride on acid side of isoelectr. point	basophilic sodium gelatin on alk. side of isoelectr. point	saline + soln.
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The biological importance of this model is not yet established.

5. Little is known about the chemical composition of those tissue structures which show differential staining, but the makeup of the analogous artificial model systems is so thoroughly understood that the physical nature of the currents can be definitely established; *phase boundary potentials* are present which are differentiated on account of a soap content of layer I and an amine chloride content of layer II, thus producing an excess of Na^+ ions in layer I and of Cl^- in layer II.

This work was carried out at the Cleveland Clinic Foundation; the writer wishes to express his appreciation to Dr. G. W. Crile for his kind interest in this work and his valuable suggestions.

BIGWOOD, E. J. (BRUXELLES). La distribution des ions dans un bloc de gelée de gélatine en état d'équilibre apparent avec une solution électrolytique minérale.

Quand des blocs de gelée de gélatine sont immergés dans une solution chlorurée calcique de pH différent de celui qui correspond au point isoélectrique de la protéine, il y a, au moment où il existe un régime stationnaire d'équilibre apparent dans le système, une distribution inégale des éléments calcium et chlore entre les deux phases aqueuses et l'équation de Donnan se vérifie *approximativement*. Mais la comparaison entre les compositions de chacun des blocs indique que les choses se passent comme si la distribution des ions n'était pas homogène dans toute la masse d'un même bloc gélatineux. L'hétérogénéité de distribution des ions dans la gelée peut être mise facilement en évidence pour les ions H^+ et OH^- et l'expérience démontre qu'il faut distinguer une région périphérique du bloc dont la composition est surtout influencée par celle de la liqueur extérieure et une région centrale dans laquelle l'effet de Donnan est dominant. L'équilibre apparent du système ne se caractérise *pas* par le schéma trop simple d'un équilibre entre deux phases homogènes séparées par une limite linéaire. L'Effet de Donnan dans le bloc de gelée se répartit progressivement dans toute l'étendue du bloc en se faisant sentir par étapes concentriques successives entre deux états extrêmes, celui du centre du bloc d'une part et celui de la solution extérieure d'autre part. Le volume relatif occupé par la zone marginale par rapport au volume total du bloc est d'autant plus élevé que l'effet de Donnan est plus prononcé.

Ces observations ne sont peut-être pas sans signification dans l'étude des phénomènes colloïdaux envisagés au point de vue de la théorie de Loeb et aussi dans l'étude des différences de propriétés protoplasmiques que Chambers a notées, par micromanipulations, entre le centre et la périphérie de certaines cellules.

¹ J. Loeb. *Proteins and Theory of Coll. Behav.* New York, 1922.

BILLARD, G. et P. DODEL (CLERMONT-FERRAND). Sur les phénomènes de phylaxie.

Certaines neurotoxines, injectées à l'animal quelques minutes avant une autre substance neurotoxique, empêchent l'apparition des accidents dus à cette seconde substance. Ces faits, observés un grand nombre de fois, constituent les phénomènes de phylaxie.

Les auteurs étudient les conditions d'apparition du phénomène et son mode intime d'action.

BILLS, C. E., E. M. HONEYWELL, W. M. COX, JR., and A. M. WIRICK (EVANSVILLE). Studies on the Activation of Ergosterol.

By shaking a chloroform solution of ergosterol with aqueous hydrobromic acid in the dark one obtains isoergosterol of greater purity than the product described by Reindel. A mixture of isoergosterol, 40 parts, and ergosterol, 60 parts, gives an absorption spectrum practically identical with the spectrum of ergosterol which has been slightly over-irradiated in alcohol. Nevertheless, this mixture exhibits no antirickettic action, in spite of the presence of a strong band at 248 m μ . It follows that biological assay is the only means at present available for studying the formation and decomposition of vitamin D. By an improved assay method it has been found that time is not the only factor in the activation of ergosterol in transparent solvents. There is also a constant specific to the solvent employed, so that when ergosterol is activated in alcohol, ether, or cyclohexane, the curve of potency plotted against time differs greatly according to the solvent. Indeed, a freely transparent solvent is not always required, for extremely high activation can be obtained in arachis oil, which is the solvent employed in commercial practice. Extensive tests with rats show that the activated ergosterol is remarkably non-toxic, 4000 to 40,000 times the therapeutic dose being required to produce hypercalcification in long-time experiments.

BINET, LÉON et R. GAYET (PARIS). Action de l'asphyxie sur les centres vaso-moteurs supérieurs; méthode de la tête perfusée.

Si l'on irrigue la tête d'un chien B, dont les artères vertébrales ont été ligaturées antérieurement, par les carotides d'un chien A (anastomose carotido-carotidienne), on observe, en asphyxiant A, une hypertension nette chez A et une hypotension chez B.

Si on a eu soin de détruire chez B les nerfs du sinus carotidien, à droite et à gauche, on note sous l'influence de l'asphyxie de A, une hypertension nette chez A et aussi chez B.—Si l'on a détruit le nerf carotidien d'un seul côté, chez B, et si on asphyxie A, on note alors, chez B, une hypotension quand on a comprimé antérieurement la carotide éternée, une hypertension lorsqu'on a pincé au contraire la carotide normale—Enfin, si au lieu d'anastomoser carotides à carotides, on anastomose les carotides de A avec les vertébrales de B, l'asphyxie de A déclenche une hypertension chez B.

Ainsi, lorsqu'on perfuse la tête d'un chien B par un chien A et qu'on asphyxie ce dernier, l'effet produit sur la pression de B est la résultante de deux actions: d'une part, l'action mécanique de la variation de pression qui se communique de A au système carotidien de B et qui, par un mécanisme réflexe détermine chez celui-ci une variation de sens opposé; d'autre part, l'action directe, chimique, du sang asphyxique sur les centres

supérieurs de B. De ces deux actions, la première prédomine et empêche l'autre de se traduire. Par une destruction du nerf carotidien, on peut éluder la première et alors l'action chimique du sang asphyxique se traduit avec pureté par de l'hypertension.

BISCHOFF, FRITZ and L. C. MAXWELL (SANTA BARBARA). Reaction of Lead with the Erythrocytes.

Injections¹ of large amounts of colloidal tri-lead phosphate into the blood stream produce no symptoms of anemia over a long period of time. Injections² of small amounts of ionizable lead salts produce severe symptoms of anemia, even though there is present in the blood plasma a great excess of inorganic phosphate over that required to convert all the ionizable lead to tri-lead phosphate. When lead acetate is added to plasma,³ a double lead calcium phosphate is formed, which is no more destructive to the red cells than lead phosphate. The damage resulting from the injection of ionizable lead salts, therefore, must be due to the reaction of the lead ion with some other constituent of the red cells than the phosphate.

By treating the ultrafiltrate from washed, hemolyzed red cells with known amounts of lead, it was demonstrated by analyses of the phosphorus removed that some compound other than tri-lead phosphate is formed, even though less lead than the theoretical amount to form the tri-phosphate was used. Similar results were obtained from the unhemolyzed cells. The great rapidity with which the inorganic phosphorus changes in red cells made it necessary to study the hydrolysis rate under various conditions. Some other compound was formed even when the inorganic phosphorus resulting from hydrolysis, which was considerably higher than the initial value, had reached equilibrium. The compound gives negative Molisch, biuret, and α -naphthol guanidine tests, and appears to be identical or related to Greenwald's diphosphoglycerate.

BLAIR, E. A., C. E. KING and W. E. GARREY (NASHVILLE). Inspiratory Irradiation.

Along with the well known respiratory hippus and changes in cardiac rate accompanying breathing movements, we have observed marked variations in reflexes and activities involving the skeletal musculature.

1. There is an augmentation of the knee-jerk and the Achilles reflex during inspiration. This has been demonstrated in both man and the dog. No change in reflex response has been shown during expiration. This result is not modified by section of both vagi in the mid-cervical region, but is abolished by transection of the cord in the upper lumbar region. There is some variation in the time relations between maximal augmentation and the inspiratory movements, recorded mechanically. In a few cases the maximal augmentation occurred during the later phases of inspiration.

2. There is an inspiratory scratch reflex after-discharge. This was demonstrated and studied in decerebrate cats. During the application of the stimulus the rate and the intensity of the movements are maintained at

¹ Bischoff, F. and N. R. Blatherwick. Journ. Pharm. Exper. Therap., 1927, xxxi, 361.

² Bischoff, F. and N. R. Blatherwick. Journ. Pharm. Exper. Therap., 1927, xxxi, 27.

³ Bischoff, F. and L. C. Maxwell. Journ. Biol. Chem., 1928, lxxix, 5.

a constant level. On discontinuance of the stimulation the movements die out rapidly, appearing in groups during inspiration and disappearing completely after three or four respiratory movements.

3. There is a marked augmentation of shiver during inspiration. This was observed and studied in animals anesthetized with barbital. Animals so anesthetized frequently shiver violently when disturbed or when cooled. At the onset of the shiver the movements appear only during inspiration, later when they become continuous there is a marked inspiratory augmentation. In one animal the augmentation in the fore limbs visibly preceded that in the hind limbs.

4. A definite inspiratory augmentation of tetany in parathyroidectomies has been observed and recorded.

The observations above noted are interpreted to mean that the impulses emanating from the respiratory center during inspiration "irradiate" down the cord. This results in an increase in excitability of the neuromuscular mechanism, manifested by inspiratory augmentation of continuous activities, and of reflexes elicited at the proper time.

BODANSKY, MEYER, EDWARD H. SCHWAB and PAUL BRINDLEY (GALVESTON, TEXAS). Creatine Metabolism in a Case of Generalized Myositis Fibrosa.

Marked creatinuria, even on a creatine-free diet, an almost complete inability to store exogenous creatine, and a low creatine content of the muscles were the outstanding features observed in a case of generalized myositis fibrosa in a 15 year old boy.

When compared with normal individuals, from infancy to adult age, the failure to store creatine for an indefinite period was found to be very striking. However, a transitory type of storage was indicated from the observations that the administration of creatine did not lead to an accumulation of creatine in the blood (in contradistinction to the behavior of creatinine); that it was not eliminated at once, but required from 24 to 48 hours to be excreted; that a small portion was converted into creatinine.

The abnormality of the creatine metabolism in this disease seemed to be due not to an inability to convert creatine into creatinine, but primarily to a failure to store creatine. The results obtained support the view that the formation of creatinine from creatine is not a direct process but depends on the preliminary storage of the creatine in the muscles in some form that is not easily liberated.

The creatine content of the muscles showed a relationship to the severity of the anatomical changes, particularly to the amount of inflammation. Thus the soleus, which appeared most normal and showed least inflammation and fibrosis, contained more creatine (324 mgm. per 100 grams) than any of the muscles analyzed. On the other hand, the iliacus and deltoid, which showed a great deal of inflammation and fibrosis were very low in creatine content (160 mgm. per 100 grams of iliacus and 204 mgm. per 100 grams of psoas).

DE BOER, S. (AMSTERDAM). New Experiments upon the Rhythm of the Tortoise Heart.

The following experiments which were performed with the heart of the tortoise will be shown and explained.

1. Recurring systoles of the ventricle after an induction shock of the auricles. The auricles pulsate at the same frequent rhythm. It will be proved that the A - V tachycardia is not present.

2. After an induction shock of the auricles auricular and ventricular tachycardias arise. Between both tachycardias no connection exists.

3. Ventricular tachycardia, induced after an extrasystole of the auricles. The tachycardia stops and starts again after a normal sinus excitation.

4. Extrasystoles of the auricles which are followed by two compensatory pauses.

5. Interpolated extrasystoles of the auricles.

6. The staircase phenomenon of Bowditch after a postcompensatory systole of the auricles. This staircase arises when the height of the postcompensatory systole has diminished.

BOLDYREFF, W. N. (BATTLE CREEK, MICHIGAN). Disturbance of the Acid-Base Balance in Stomach and Small Intestine as a Cause Producing Anemia.

In the stomach during digestion HCl is found in strong solution (up to 0.5 per cent), while in the duodenum its content is below 0.1 per cent (N. A. Milovzoroff).

The fact that acid is not absorbed from the stomach and may be easily absorbed from intestine gave the author an idea that its entry into the blood would be detrimental for the red corpuscles of the blood; as it is known that acids destroy them *in vitro*. Hence, the excess of acid in the intestine may cause anemia. If this idea is correct then neutralization of acids in the stomach by the alkali of the pancreatic juice is intended outside of other reasons also to prevent the destructive effect of acids on erythrocytes.

Experiments of Ephraim Boldyreff in the author's laboratory on 7 fistular dogs with the introduction of acids into the stomach and various regions of the small and large intestine, as well as on the dog with the ligation of both pancreatic ducts, showed that acids are quickly absorbed into the blood from any part of the intestine (10-15 minutes from Thiry-Vella fistula) and in $1\frac{1}{2}$ to 4 hours are capable of decreasing the number of erythrocytes in the blood by from 1,000,000 to 2,000,000.

Repeated excessive introductions of 0.5 per cent HCl or 1.25 per cent $C_3H_5O_3$ (up to 200-400 cc. daily) into the stomach already in 2-3 weeks caused a drop of erythrocytes of more than 1,000,000 with the appearance of pathological forms. Cessation of such introductions brought the cell count to normal in several weeks.

Thus, the excess of acids in the digestive apparatus produced by any cause (excess of acid secretion, deficient neutralization, acid production from the food, etc.) in any part of the digestive canal is followed by the advent of anemia resembling the anemia of pernicious type.

BOLDYREFF, W. N. (BATTLE CREEK, MICHIGAN). External and Internal Secretions of the Pancreas and their Interrelation.

As was shown by my former experiments (Kazan, Russia, 1914) and new investigations under sterile conditions, by Ephraim Boldyreff in my laboratory (Battle Creek, Michigan, 1928), the pancreatic juice contains a strong glycolytic ferment which splits glucose *in vitro* with formation of lactic acid.

The administration of zymogen pancreatic juice into the blood of animals is easily tolerated without any harm to them (dogs of 15-20 kilo—20-30 cc.). The same dosage of active juice kills the animals in one to two days with the same uniform picture of general poisoning.

Under normal conditions the ferments of the pancreatic juice is quickly absorbed into the blood (experiments of the author, Kniazeff, and others).

The exclusion of pancreatic juice from the intestine (ligation of the ducts, pancreatic fistula, pancreatectomy) causes an increase of blood sugar content (our data for all three cases and literary data for the third case).

Literary data show that substances stimulating pancreatic secretion lower the blood sugar level.

Experiments of Ephraim Boldyreff showed that absorption of pancreatic juice by the blood is followed by a drop in the blood sugar.

The above related data permit the conclusion to be made that pancreatic juice (external secretion) in normal conditions enters the blood and does there (partly or entirely) the work of breaking down of sugar which is ascribed to the action of internal secretion. The author does not believe that the impossibility of the secretion of the islands of Langerhans to enter the intestine with the external pancreatic secretion is proven. Pancreatic preparations (Banting, Macleod, von Noorden, and others) and pancreatic juice (Boldyreff, Hedon) in depancreatized animals and in diabetics assist the action of insulin.

Therefore, the external pancreatic secretion may serve as an important remedy in the clinic in cases of pancreatic afflictions as an addition to insulin and other proven means of treatment.

BOOTHBY, WALTER M. and IRENE SANDIFORD (ROCHESTER, MINNESOTA).

Normal Values of Basal or Standard Metabolism. A Modification of the DuBois Standards.

Basal or standard metabolic rates have been made in our laboratory on more than 60,000 individuals, up to December, 1926. From this number we have selected 6,888 subjects (1,822 males, 5,066 females) who on careful physical examination revealed no abnormalities which would influence their rate of heat production. Included in this series are the 262 school children to be reported by Sandiford and Harrington.

The data are expressed on the basis of calories per square meter referred to age for both males and females using the height-weight formula of DuBois and DuBois for the following reasons: 1. DuBois was the first to develop a practical clinical standard of heat production. 2. The statistical treatment of our series supports the accuracy of the original DuBois standards being only 1 to 4 per cent lower for the adults and 3 to 7 per cent lower for children down to the age of fourteen. 3. The utilization of the height-weight factors combined to represent surface area and the adoption of standards on the basis of age for each sex has the great advantage of indicating simply and clearly the difference in the rate of the basal metabolism between men and women. 4. This method of expression likewise clearly shows the rapid decrease in rate of the basal metabolism of male children between the ages of five and twenty-one and the more rapid decrease in female children between the ages of five and seventeen followed

in both sexes by a gradual and nearly parallel decline to old age. 5. Finally, it permits of the correlation of the rapidly decreasing heat production from infancy to maturity and the more slowly decreasing heat production of adult life on the basis of the phenomena of intra-cellular motion, inevitably accompanied by increased heat formation, associated with the act of mitotic cell division.

The DuBois Normal Standards as modified by Boothby and Sandiford
Calories per square meter per hour

AGE	MALES	FEMALES	AGE	MALES	FEMALES
5	(53.0)	(51.6)	20-24	41.0	36.9
6	52.7	50.7	25-29	40.3	36.6
7	52.0	49.3			
8	51.2	48.1	30-34	39.8	36.2
9	50.4	46.9	35-39	39.2	35.8
10	49.5	45.8	40-44	38.3	35.3
11	48.6	44.6	45-49	37.8	35.0
12	47.8	43.4			
13	47.1	42.0	50-54	37.2	34.5
14	46.2	41.0	55-59	36.6	34.1
15	45.3	39.6	60-64	36.0	33.8
16	44.7	38.5	65-69	35.3	33.4
17	43.7	37.4			
18	42.9	37.3	70-74	(34.8)	(32.8)
19	42.1	37.2	75-79	(34.2)	(32.3)

In using table the age should be determined to the nearest year. That is, 4 years 6 months to 5 years 5 months inclusive, is taken as 5 years; to do this correctly the actual birthday must be known and is important for children. The DuBois height-weight formula for surface area was used.

BORODIN, D. N. (RUSSIA). **Demonstrations on Mitogenetic Rays.**

BOTTAZZI, FIL. (NAPLES). **Tensione Superficiale delle Soluzioni Proteiche.**

Si è determinata la tensione superficiale dinamica e statica di soluzioni di sieroalbumina e di ovoalbumina a lungo dializzate, in concentrazioni piuttosto piccole (0,3-0,001%), a vario pH, servendosi dell'apparecchio di Le Compte Du No. y. Il pH è stato misurato elettrometricamente con l'elettrodo a idrogeno. Dall'esame dei risultati si può trarre la conclusione dell'esistenza di un minimo di tensione superficiale sia dinamica, sia statica, in corrispondenza del punto isoelettrico delle rispettive proteine. Questo dato conferma i risultati precedenti delle ricerche di Bottazzi e collaboratori sulla tensione superficiale delle soluzioni proteiche. La differenza fra i valori di tensione superficiale dinamica e statica, al punto isoelettrico, varia da 6 a 11 dine/cm.

Con la sieroalbumina poi si son fatte ricerche a diluizioni fortissime, tali da comprendere quella concentrazione alla quale tutta la proteina sciolta doveva disporsi in uno strato monomolecolare all'interfacie liquido-aria, e nell'altra liquido-vetro. Anche in corrispondenza di questa concentrazione il minimo di tensione superficiale si trova al punto isoelettrico. Il minimo si osserva, però, soltanto nei valori statici, non in quelli dinamici, che permangono tutti identici e uguali al valore dell'acqua distillata.

La concentrazione della sieroalbumina occorrente per la formazione dello strato monomolecolare è di 1/130,000 per una estensione totale dell'interfacie uguale a 44,35 cmq. L'abbassamento di tensione superficiale statica, che si osserva al punto isoelettrico, oltre il minimo dovuto alla formazione dello strato monomolecolare (abbassamento di circa 4 dine/cm), non è dovuto al portarsi di altre molecole tensioattive all'interfacie, poichè lo strato era e resta monomolecolare, cioè non è dovuto a variazione di numero di molecole tensioattive, ma è dovuto a un aumento del potere tensioattivo di ciascuna molecola. Questo risultato conferma quanto da tempo era stato ammesso da Bottazzi, e cioè:

1. Le proteine abbassano la tensione superficiale dell'acqua solo quando si trovano allo stato di dispersione molecolare;

2. Al punto isoelettrico il potere tonomeiotico delle molecole di proteine solubili raggiunge un valore massimo. Ciò è da imputarsi a diminuzione del grado di ionizzazione.

BOUCKAERT, J. J. (GHENT and CHICAGO). Hyperthermia, Liver Glycogen and Blood Sugar after Injection of β -Tetrahydronaphthylamine in Dogs with Normal and Denervated Liver.

We showed previously, in collaboration with C. Heymans, that the hyperthermia induced by β -tetrahydronaphthylamine can still be observed in thyro-parathyroidectomised dogs, in adrenalectomised dogs, or in dogs having undergone both operations. Hyperthermia after injection of β -tetrahydronaphthylamine also occurs in splanchnotomised dogs.¹ In the latter case, and also after adrenalectomy, we find hypoglycemia instead of hyperglycemia which usually follows an injection of β -tetrahydronaphthylamine. In later experiments² we observed that hepatectomised dogs, although being apparently in good general condition, do not present any hyperthermia after injection of β -tetrahydronaphthylamine. The liver thus seems to play a predominant part in the production of naphthylamine-hyperthermia. In another series of experiments, we examined the rôle played by the liver nerves in the phenomenon of hyperthermia. For this purpose, we injected hyperthermic doses of β -tetrahydronaphthylamine in dogs which had previously undergone denervation of the liver. We observed then (as also mentioned by Borchardt for cats³) that those dogs present hyperthermia after injection of β -tetrahydronaphthylamine. However, instead of a hyperglycemia normally following the injection, there is a hypoglycemia that may be sometimes very marked: in one of our dogs we had a hypoglycemia of 0.31 per cent.

It is a known fact that the injection of β -tetrahydronaphthylamine normally provokes a liberation of liver glycogen and consequently a hyperglycemia. Is the hypoglycemia that one can observe in dogs with denervated liver and injected with β -tetrahydronaphthylamine due to a defect of liver glycogen liberation? To clear up this point, we made some determinations of liver glycogen on dogs with denervated liver, before and after injection of β -tetrahydronaphthylamine. We observed that in these animals, hyperthermia is still accompanied by a very marked decrease of

¹ Jean J. Bouckaert et C. Heymans: C. R. 2e Reunion Ass. des Physiol. Bruxelles, 16-18 juillet 1928-Ann. de Physiol. et de Physioch. biol. iv, p. 654, 1928; Arch. intern. Pharmacod. et de Therap., xxxv, p. 153, 1928.

² Jean J. Bouckaert: C. R. Soc. Biol., c, p. 769, 1929.

³ W. Borchardt: Arch. f. exp. Path. u. Pharm., cxxxvii, p. 45, 1928.

liver glycogen. The same thing is to be observed on dogs who have undergone denervation of the liver and of the adrenals.

There is evidence that after adrenalectomy, the hypoglycemia following the injection of β -tetrahydronaphthylamine is less than after splanchnotomy or denervation of the liver. One might think therefore that the above drug acts on the liver directly and by way of the splanchnic nerves, liberating glucose, and that it also acts on the adrenals, more adrenalin being produced and, in consequence, a somewhat higher production of glucose by the liver taking place.

BOUCKAERT, J. P. (LOUVAIN). Internal Friction in Muscle.

Registering the shortening of a muscle as a function of time after a sudden unloading, it is possible to confirm the view that the muscle in the contracted state is mechanically equivalent to a system composed of two springs, one damped and one undamped. The values of the various constants have been calculated and their significance will be discussed.

BOUCKAERT, J. P. (LOUVAIN). Internal Friction in Muscle. (Demonstration)

BOUISSET, L., L. BUGNARD et L. C. SOULA (TOULOUSE). La régulation cholestérolémique dans le poumon.

Pendant la traversée du poumon, le sérum sanguin s'appauvrit en cholestérol. Le fait a été mis en évidence par nous mêmes. La différence en faveur du sang veineux est assez variable de 0.15 gr à 0.33 gr par litre. Nos expériences sur la polypnée et l'asphyxie ont montré que l'appauvrissement du sérum en cholestérol au niveau du poumon est accru par l'augmentation de la ventilation, diminué par l'arrêt de l'hématose.

Nous avons dosé le cholestérol non plus dans le sérum mais dans le plasma obtenu par centrifugation de sang oxalaté recueilli à l'abri de l'air, et dans le sang total. La détermination du rapport: $\frac{\text{Vol. des globules}}{\text{Vol. du sang total}}$ permet alors d'obtenir par un calcul simple la teneur en cholestérol des globules. Ces déterminations ont été faites sur du sang artériel recueilli à la canule carotidienne et sur du sang veineux prélevé dans le coeur droit par une sonde jugulaire.

Nous avons toujours constaté que la traversée pulmonaire s'accompagnait d'un appauvrissement du plasma en cholestérol et d'un enrichissement des globules alors que la teneur en cholestérol du sang total variait peu.

Nous avons toujours trouvé une disparition de cholestérol dans le plasma et une augmentation dans les globules. La traversée pulmonaire s'accompagne d'un appauvrissement en cholestérol de la partie liquide du sang et d'un enrichissement des éléments figurés. La teneur en cholestérol du sang total subit, elle, des variations peu importantes et généralement en faveur du sang artériel. Il semble donc que les variations dans la teneur en cholestérol du sérum au niveau du poumon correspondent à un simple déplacement de ce lipide du plasma aux globules. Certains auteurs ont mis en évidence le déplacement de l'ion Cl des globules vers le sérum pendant la traversée pulmonaire et le rôle de ce déplacement dans la régulation du P.H. Nous croyons que les mouvements du cholestérol que nous avons observés ressortissent à un mécanisme analogue.

Nous avons cherché à reproduire "in vitro," le déplacement du cholestérol en fonction de la pression du CO_2 dans le sang. Nous avons prélevé *sous huile* du sang artériel carotidien en le rendant incoagulable par addition de citrate de soude. Dans un premier lot de sang on fait passer un courant de CO_2 , dans un deuxième lot un courant d'oxygène; un troisième lot est gardé comme témoin. Ces barbotages doivent être effectués sous de faibles pressions et ne pas entraîner d'hémolyse. Le déséquilibre causé par le barbotage des gaz entraîne une mobilisation du cholestérol des globules vers le plasma lorsqu'on introduit un excès de CO_2 , en sens inverse dans le cas d'un excès d'oxygène.

Nous concluerons de ces recherches à l'existence d'une régulation pulmonaire de la cholestérolémie effectuée par le tissu sanguin lui-même. Sous l'influence des nombreux facteurs qui règlent l'équilibre physico-chimique du sang, (en particulier l'anhydride carbonique et l'oxygène) le cholestérol passe des éléments figurés dans la partie liquide ou inversement. Cet enrichissement globulaire en cholestérol au niveau du poumon augmente la résistance globulaire et réalise une véritable remise à neuf du globule, au moment où il va être repris par la circulation générale. L'importance de la participation du cholestérol au maintien de l'équilibre physico-chimique du sang découle de ces faits. La Cholestérolémie du plasma est sous la dépendance étroite de la teneur en CO_2 .

BOURGUIGNON, GEORGES (PARIS). Chronaxies normales des terminaisons servitires cutanées chez l'homme.

N'ayant pas réussi à mesurer la chronaxie des terminaisons nerveuses de la peau avec la méthode monopolaire, j'ai essayé la méthode bipolaire avec une électrode impolarisable constituée par deux pointes d'argent chlorurées électrolytiquement et maintenues à une très courte distance, 3 millimètres environ, l'une de l'autre, par un manchon d'ébonite. Un léger degré d'humidité est maintenu en entourant la base de chaque pointe de 2 ou 3 tours de fil de lin imbibé d'une solution de NaCl à 4 pour 1000.

Avec cette électrode, qui réduit au minimum la diffusion du courant, la sensation éveillée par l'excitation électrique est, suivant sa situation, une sensation de *choc*, une sensation de *fourmillement* ou une sensation de *chaleur*.

À la sensation de choc correspond une chronaxie égale à celle des muscles sous-jacents (isochonisme sensitivo-moteur); à la sensation de fourmillement correspond une chronaxie 5 fois plus grande et à la sensation de chaleur une chronaxie 10 fois plus grande que la première. Du volume relatif des terminaisons on peut inférer que probablement la petite chronaxie est celle des corpuscules de Pacini, organes probables de la sensibilité tactile; que la chronaxie moyenne est celle des corpuscules de Meissner, qui seraient ainsi les organes de la sensation de fourmillement, qui se transforme en sensation douloureuse quand le courant est très intense; et que la grande chronaxie serait celle des terminaisons libres intra-épidermiques, qui seraient ainsi les organes de la sensibilité à la température, comme on l'a déjà dit.

Dans les troncs nerveux, on ne trouve que les deux premières chronaxies: je n'ai pu y déceler ni la sensation de chaleur ni la plus grande chronaxie. Les sensations thermiques paraissent donc passer par les nerfs sympathiques à qui appartiendraient les terminaisons libres intra-épidermiques, comme on l'a déjà soutenu.

BOURGUIGNON, GEORGES (PARIS). **Démonstration d'une table pour la mesure de la chronaxie chez l'homme et chez les animaux. Expérience de mesure de la chronaxie normale du nerf vestibulaire de l'homme.**

L'auteur expose la constitution de la table qu'il a fait construire par la maison A. Walter pour la mesure de la chronaxie chez l'Homme et chez les animaux.

Il présente ensuite l'électrode biauriculaire impolarisable (en argent chloruré électrolytiquement) qu'il a fait établir pour la mesure de la chronaxie du nerf vestibulaire.

La fermeture brusque du courant continu ou les décharges de condensateurs déterminent une inclinaison brusque de la tête du côté de l'oreille dans laquelle se trouve le pôle positif. On peut ainsi mesurer la chronaxie du nerf vestibulaire.

Chez l'Homme normal, quand les deux électrodes sont bien symétriquement placées, les rhéobases et les chronaxies sont rigoureusement égales à droite et à gauche.

Les valeurs normales de la chronaxie vestibulaire de l'Homme sont comprises entre 14σ et 22σ . Tandis que, dans les muscles et les nerfs moteurs et sensitifs généraux, on ne peut mettre en évidence avec certitude des différences individuelles, on met facilement en évidence des différences individuelles dans le nerf vestibulaire. On peut diviser les sujets normaux en 2 catégories, suivant qu'ils ont une chronaxie vestibulaire petite (14σ à 18σ), ou grande (18σ à 22σ).

Sur les sujets examinés à ce point de vue, les sujets à petite chronaxie vestibulaire sont des émotifs, tandis que les sujets à grande chronaxie vestibulaire ne sont pas des émotifs. Pour généraliser cette proposition, il faut que les expériences soient plus nombreuses. Dès maintenant cependant il apparaît bien que la chronaxie vestibulaire fournit une caractéristique individuelle.

BOZLER, EMIL (MÜNCHEN). **Heat Production in Smooth Muscle.**

Measurements were made in the laboratory of Hill with his myothermic method. The retractor of the pharynx of *Helix pomatia* proved to be very suitable for this method, as it is straight fibred, in shape like a sartorius and because it can be stimulated with very weak electrical stimuli.

Results: $\frac{T_1}{H}$ is on the average for short duration of stimulus 6.9, increasing for longer duration proportional to the time of stimulation. The total heat consists of initial and recovery heat; the ratio is on the average 1:1.01. The recovery heat appears only in the presence of oxygen. These measurements agreeing so strikingly with those for frog sartorius suggest that the mechanism of contraction is in both cases the same. Maintaining of tension is always accompanied by heat production, during contraction produced by electrical stimulation as well as during all kinds of spontaneous contractions. The amount of heat produced, however, is not constant. The muscle spends at first comparatively much energy for maintaining a tension. But if the contraction continues, the muscle becomes gradually many times more economical. This change is accompanied by a change in the time relations of the mechanical response, similar to that of skeletal muscle during fatigue, but occurring much faster and reaching a much greater extent. The relaxation time of the same muscle

can change from 4 seconds to several minutes. It is believed that these facts fully explain the great economy for maintaining a tension peculiar to smooth muscle without postulating any special catch mechanism.

BOZLER, EMIL (MÜNCHEN). **Heat Production in Smooth Muscle.** (Demonstration)

BRACK, W. (BASEL). **Über den Unterschied zwischen normalen und abnorm eingestellten autonomen Funktionen beim Menschen.**

Während auf das Trinken einer Tasse Milch bei Normalen keine Veränderungen von Kalium und Calcium im Blut konstatierbar sind, findet man solche Veränderungen stets bei Patienten mit abnorm eingestellten autonomen Funktionen.

Werden *Normale* durch spezifische Mittel vorbehandelt, so tritt dasselbe ein. Dabei wurde gefunden, dass nach Vorbehandlung mit dem gleichen Mittel der Ablauf der K-Ca-Schwankungen stets ein gleichartiger ist (während er nach Injektionen desselben Mittels ganz verschieden ausfällt). Die Vorbehandlung mit verschiedenen Mitteln (geprüft wurden Ergotamintartrat, Methyl- und Allylyohimbin und Pilocarpinhydrochlorid) gibt dagegen ganz verschiedene Resultate.

Wir haben damit eine Methode um die statische Wirkung solcher Medikamente beim Menschen an einer einzelnen—im Zusammenhang mit dem übrigen Organismus gebliebenen—Funktion zu prüfen und die Wirkungen miteinander zu vergleichen.

Bei *Patienten mit abnorm eingestellten Funktionen* verhalten sich die K-Ca-Schwankungen ganz verschieden. Nach ihrem Ablauf und ihrer Beeinflussbarkeit habe ich 3 verschiedene Reaktionstypen unterschieden: *sympathikotonische* Reaktionen werden durch negativ sympathikotrope und positiv parasymphatikotrope Mittel aufgehoben und durch positiv sympathikotrope und negativ parasymphatikotrope verstärkt; *parasymphatikotonische* Reaktionen verhalten sich den gleichen Mitteln gegenüber gerade entgegengesetzt. *Normalüberempfindliche Reaktionen* verhalten sich gleich wie normale, nur besitzen sie eine grössere Ansprechbarkeit.

Das gleiche Mittel kann demnach ganz verschiedene Wirkung zeigen, je nachdem es bei Patienten mit verschiedenen Reaktionen geprüft wird.

Ferner hat die Prüfung von Ergotamintartrat, Methyl-yohimbin und Pilocarpinhydrochlorid bei derselben Patientin mit sympathikotonischer Reaktion ergeben, dass diese 3 Mittel bei Menschen mit abnormen Funktionen völlig gleichartig wirken können.

Der *Vergleich* zwischen normalen und abnormen Funktionen ergibt: normale Funktionen reagieren auf gleiche Reize gleich, abnorme dagegen verschieden. Verschiedenartige Reize, die normale verschieden beeinflussen, können auf abnorme völlig gleich wirken.

Die Bedeutung von Qualität und Intensität (frühere Versuche) der Reize tritt somit bei abnormen Funktionen zu Gunsten der abnormen Funktionsbereitschaft weitgehend zurück.

BRAND, E., M. M. HARRIS, M. SANDBERG and A. I. RINGER (MONTEFIORE HOSPITAL, NEW YORK CITY). **Studies on the Origin of Creatine.**

Cases of progressive pseudohypertrophic muscular dystrophy have marked creatinuria, and creatine orally administered to them is promptly

and almost quantitatively eliminated in the urine. These cases are, therefore, more suitable than normal beings for studies on the origin of creatine.

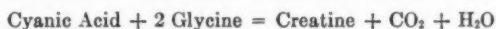
For about one and a half years five patients with this disease have been kept on standard purine and creatine free diets of constant nitrogen, phosphorus and sulfur content. Their urine was analyzed daily for creatinine, creatine, urea, ammonia, uric acid, amino acid and total nitrogen, inorganic P, total S (sulfur partition in 30 periods). During experimental periods, amino acids (in amount corresponding to between 1 and 2 grams of N daily) and other substances were given in addition to the diet. There were 74 experimental and 66 control periods, varying in duration from 1 to 3 weeks.

Glycine experiments showed an increased creatine excretion up to 40 per cent above the control level, which increase was equivalent to a transformation of 4-8 per cent of the glycine. During these experiments the sulfur excretion dropped and the extra nitrogen eliminated was less than that given as glycine. This nitrogen and sulfur sparing effect of glycine continued for more than a month in the after period. The transformation of glycine into creatine was further confirmed by the drop in creatine excretion following benzoic acid and sodium benzoate feeding.

Glycine + *D*-arginine produce no greater creatinuria than glycine alone. Guanidoacetic acid produces large amounts of creatine.

There was a slightly diminished creatine excretion with sodium acetate and a slightly increased excretion with ammonium chloride, sarcosine, *i*-alanine and *D*-arginine. Nucleic acid, urea, lactic acid, uric acid, *D*-glutaminic acid, *l*-histidine, *l*-tyrosine and *l*-cystine were practically without effect on creatine excretion. Betaine produced an increased creatine excretion for a few days, which then dropped below the control level in spite of continued feeding.

On the basis of the cyanic acid theory of Salkowski-Werner-Fosse creatine may possibly arise from a side reaction between cyanic acid and glycine:



BREMER, FREDERIC (BRUSSELS). The Summation of Nervous Impulses.

Summation (*addition latente*) of nervous impulses has been studied in three different conditions where a single maximal break-shock on the nerve had no visible effect, while two such stimuli, properly timed, caused a contraction: light curarisation of the skeletal muscle of the frog and of the cat; advanced fatigue of the same muscles; myotonic condition (aptitude to neuro-muscular contracture) of the brown frog (*Temporaria*).

In all these cases the effectiveness of the summation of two volleys of impulses has been found to depend, in a characteristic manner, upon the time interval of their arrival at the neuro-muscular junction. The curves giving in ordinates the height of the contraction (ordinary twitch or slow secondary contraction) produced by the 2nd impulse on the intervals of the two stimuli in abscissae, are all of the same shape. The comparison with them of the recovery curves of the nerve, shows that summation begins to be visible very soon after the recovery of the nerve fibers from the absolute refractory period allows the elicitation of a second impulse (*minimal interval*) and that it is effective in an increasing number of neuro-muscular units, up to an *optimal interval*, then is less and less manifest and

ceases to be visible at a *maximal interval*, which varies with the phenomenon studied and with the condition of the neuro-muscular preparation.

The situation of the optimal interval within the relative refractory period of the nerve excludes the hypothesis that summation depends on the development of a supernormal period of the nerve fibers.

The characteristic features of the summation curve may be explained by the assumption that neuro-muscular "transmission" is the *excitation* of the muscle fibers (or of a special junctional tissue) by the action currents of the nerve fibers supposed to be identical with the nervous impulses. Summation of nervous impulses would be then a summation of subliminal electrical stimuli at the neuro-muscular junction. The success of the 2nd impulse would be a function of: 1° the residual excitation left at the junction by the 1st impulse; 2° the E.M.F. of the 2nd impulse; 3° the degree of subliminality of the single impulse in each particular case.

The consideration of these three factors gives a satisfactory account of the existence of an optimal interval for summation and of the variable magnitude, in the different cases, of the maximal interval.

The validity of this explanation is strengthened by experiments where the nerve under the electrodes, or the muscle, are independently cooled or warmed. These experiments show that the optimal and maximal intervals for summation are modified by changes of temperature of the muscle and of the nerve termination within it, but not by changes of temperature of the nerve fibers at the site of the excitation, which modify only the minimal interval.

BREMER, FREDERIC (BRUSSELS). Demonstration.

BRISCOE, GRACE (LONDON). The Experimental Coördination of Muscular Movement. Cinematograph demonstration of muscular coördination in peripheral preparations.

New method of electrical stimulation giving control of contraction, of relaxation and of postural contraction.

Grading of rate of movement and of amplitude of movement shown.

Method of reciprocal stimulation applied to nerves of antagonistic muscles, resulting in controlled movement and posture of the limb.

Reciprocal stimulation applied to nerves of symmetrical muscles, resulting in alternate movements of the limbs or stepping action.

BRITTON, S. W. (UNIVERSITY, VIRGINIA). An Apparent Influence of Sympathetic Nerves on Muscle Glycogen.

It was considered that the sympathetic nervous system might be concerned in glycogen equilibrium in muscle, perhaps as the splanchnics are in some way related to hepatic glycogen and the sympatho-mimetic (medulliadrenal) tissues are to both muscle and liver glycogen changes. The fore and hind limb muscles on one side were sympathectomized in the cat by unilateral excision of the stellate ganglion and the abdominal sympathetic trunk. Animals examined at various times within the first few weeks post-operatively showed insignificant differences in glycogen content of the sympathectomized muscles. To avoid the vascular changes due to the denervation, studies were made chiefly from 10 to 13 weeks after operation. At this time fairly marked increases in glycogen over the normal percentage were observed in the fore limb muscles on the

operated side, whereas in the hind limb there were found correspondingly significant diminutions in glycogen content. An explanation of the results was suggested by the post mortem observations: marked regrowth of the sympathetic nervous tissues in the region of the (excised) stellate ganglion was noted in every case (the regenerated ganglionic mass was in most instances indistinguishable in appearance from the normal), although relatively slight coordinated regrowth of the abdominal sympathetic chain was observed. In the chronic condition, sympathectomized muscle appears to suffer a diminution of its normal glycogen content. If removal of the sympathetic supply to a limb is followed, however, by reestablishment of the nervous connections, there now occurs an augmentation of the glycogen store in the muscle as compared to that on the unoperated side. The blood flow through the sympathetomized fore limb in animals killed about two months after operation was found to correspond to the normal, but was much greater than normal in the case of the operated hind limb.

BROCK, FRIEDRICH (HAMBURG). Die methodische Grundlage der Umweltforschung im Vergleich mit den wichtigsten Theorien über tierisches Verhalten.

Die Biologie kennt drei grosse Begriffssysteme, welche versuchen die tierischen Bewegungen einem einheitlichen Gesichtspunkte unterzuordnen. Der erste Versuch in dieser Richtung wurde von J. Loeb in der *Tropismentheorie* gemacht. Hier sind es vor allem die Energien der Umgebung eines Tieres, welche an seinen Sinnesorganen angreifend in gesetzmässiger Weise die Bewegungen verursachen. Sekundär werden Begriffe wie "Erregungsgleichgewicht," "Phototonus" usw. eingeführt, um Reiz, Rezeptor, Leitung und Effektor in einheitlichen kausalen Zusammenhang zu bringen.

Theorie des *Versuchs* und *Irrtums* nennt man gewöhnlich eine andere Theorie, die von H. S. Jennings aufgestellt wurde, um die mannigfaltigen tierischen Bewegungen einem Prinzip unterzuordnen. Kommt Loeb von aussen her an das Tier heran, um die Tiermaschine mit allem auszustatten, was zur physikalisch-chemischen Grundlage der Theorie nötig ist, so rückt Jennings den Organismus selbst in den Vordergrund. Jedes Tier ist ein Aktionssystem, dessen Körperbau eine bestimmte Anzahl von Bewegungsmöglichkeiten zulässt. Dieses Aktionssystem gehört aber keiner Tiermaschine an, die zwangsmässig antworten muss, sondern einem Organismus, der physiologischen Zuständen unterworfen ist. Nur im einfachsten Falle werden alle Möglichkeiten durchprobiert, um die Antwort auf die jeweilige äussere Situation zu finden, meist wirken physiologische Zustände modifizierend auf das Aktionssystem ein.

Den dritten Versuch eine Lebenstheorie aufzustellen hat J. von Uexküll gemacht, wir nennen sie die *Umwelttheorie*. Tier und bestimmte Zustände und Vorgänge seiner Umgebung (Beute, Feind, Geschlechtspartner usw.) bilden eine *Einheit* für die es gilt einen *Plan* aufzustellen. Dieser Plan umschliesst den Bauplan sowie den Funktionsplan des Tieres, welchem die auf die Komplexe der Umgebung (Feind, Beute usw.) gerichteten Bewegungen eingeordnet werden können. Diese Komplexe, welche vom Tier mittels der Sinnesorgane und des Nervensystems nach besonderen erforschbaren Gesetzen aufgebaut werden, bilden in ihrer Gesamtheit die *Umwelt* eines Tieres. Kennen wir den Tier-Umweltplan eines Lebewe-

sens, so ist es möglich jedem Verhaltensakt einen Ordnungsplatz innerhalb dieses Planes anzuweisen, wodurch die Einzelbewegung erst verständlich, sinnvoll und vorausberechenbar wird.

BROOKS, CLYDE (UNIVERSITY, ALABAMA). Blood Pressure.

Statement of epochs in blood pressure measurements.

Stephen Hales the first to measure blood pressure. Poiseuille introduced mercury manometer. Ludwig the Kymographion and with it graphic method of measuring and recording blood pressure. Marey's principle for interpreting tracings of pulsations of volume of limb and finger: a graphic method for measuring blood pressure.

Riva-Rocci's method: palpatory method introduced. Work of Korotkov introducing the auditory method. Chart showing Korotkov's entire original article in the Russian language with literal translation into English.

Experimental study showing mechanism of production of sounds produced in blood vessels of arm during blood pressure measurements with analysis of the true significance of these sounds, and their bearing on blood pressure measurements.

Study of most recent recording sphygmographic blood pressure instruments. Explanation of physical principles underlying the operation of these instruments.

Critical review of present state of knowledge of blood pressure measurements.

BROOKS, MATILDA MOLDENHAUER (BERKELEY). Penetration of Thionine into Valonia.

When *Valonia ventricosa*, a marine alga which contains a large central vacuole filled with colorless sap, is placed in sea water containing thionine (an unmethylated dye of the thiazine group related to methylene blue) thionine is found in the sap of the plant in measurable quantities. When this sap is analyzed by the spectrophotometer, absorption maxima are found at the wave lengths 559 and 600 $m\mu$, corresponding with those of the dye itself.

Since the pH of the solution used was 9.0 and the basic dissociation constant of the dye, K_b is 1.88×10^{-3} ,¹ the dye will be more than 99 per cent dissociated at this pH. It is of interest to note therefore that thionine penetrates the sap of *Valonia* as such from a highly ionized solution.

BROOKS, S. C. (BERKELEY). The Ion Permeability of Protoplasm.

Cells of *Valonia macrophysa* were placed in sea water enriched or impoverished with respect to potassium by the addition of isotonic KCl or NaCl solutions. After periods varying from one hour to seven days the sap was collected and its content of sodium, potassium and chloride determined, and compared with that of sap from similar cells which had been kept in sea water. The concentrations of potassium in the modified sea water in which the cells had been immersed ranged from one half to ten times its concentration in sea water, but changes in its concentration in the cell sap were slight even in the case of the highest potassium concentration. Slow changes in sodium and chloride concentrations also occurred. The permeability of the protoplasmic layer of this plant cell to sodium and

¹ Wm. Mansfield Clark, Barnett Cohen and H. D. Gibbs. Studies on oxidation-reduction I-X, Hygienic Laboratory Bulletin 151, Feb. 1928, p. 202.

potassium is thus shown by a direct method to be very low. The experiments support the idea that the normal state of these cells is a non-equilibrium condition in which the permeability to cations is an inverse function of their effective radius, decreasing in the order hydrogen-potassium-sodium. This idea is thus a further extension of the differential diffusion velocity schemes proposed by Andre and Demoussy¹ and by Osterhout.²

BRÜLL, LUCIEN (LIÉGE). **On the Physico-Chemical State of Inorganic Phosphate in the Plasma.**

The author used his vivi-ultrafiltration method (Compt. Rend. Soc. Biol., xcix, 1605, 1928) on the whole animal (with heparin as anticoagulant) and on Starling's heart-lung preparation, either with defibrinated blood or with heparin. In some experiments a kidney was perfused together with an ultrafilter, by means of a heart-lung.

In the experiments with heparin only a low percentage or even no inorganic phosphates were found to cross the filter.

In defibrinated blood the amount of colloidal inorganic phosphorus is much smaller, and in some cases there is none.

Increase of Ca in the plasma does not lead to a rise of the percentage of colloidal phosphorus, unless large amounts are put in (the serum Ca level must exceed ± 20 mgm. per cent).

In the heart-lung-kidney-ultrafilter preparation the inorganic phosphorus may be totally diffusible and yet the secretion of phosphates drop down to a very low level. The hypothesis put forward by Eichholz and Starling, according to which the drop of phosphorus in the urine of the heart-lung-kidney preparation might be due to a gradual change of the phosphates into a colloidal form, only holds good for cases in which large amounts of Ca are put in.

BRÜNNER-ORNSTEIN, MARTHA (WIEN). **Beitrag zur Physiologie des Oesophagus mit besonderer Berücksichtigung des Cardiospasmus.**

Nach einer kurzen Besprechung des Symptomenkomplexes des Cardiospasmus berichte ich über die pathologische Anatomie sowie über die pathologische Physiologie dieses Krankheitsbildes. Hierbei will ich mit Röntgenbildern die entzündlichen Veränderungen demonstrieren, die den idiopathischen Cardiospasmus stets begleiten. Bei dieser Gelegenheit werde ich auf die Aethiologie dieses Leidens zu sprechen kommen und mich auch mit der Differentialdiagnose gegenüber Stricturen und Stenosen, die durch Verätzungen oder durch Tumoren der Nachbarschaft hervorgerufen werden, beschäftigen. Besonders wird die Aethiologie des idiopathischen Cardiospasmus auch an Hand meines klinischen Materials genauer besprochen werden. Im Zusammenhang mit der Aethiologie soll auf die Behandlungsmethoden, die ja je nach der Aethiologie verschieden sind, und zwar die medikamentöse Therapie, die chirurgische Therapie und die Psychotherapie eingegangen werden. Schliesslich werde ich über die von mir in die Therapie eingeführte innerliche Diathermiebehandlung mit der Diathermiesonde berichten. Ich habe dieses Verfahren zuerst im Jahre 1927 von der Klinik des Professor Wagner-Jauregg aus publiziert und hatte seither Gelegenheit, ein grösseres Material zu behandeln und klinisch genau zu beobachten.

¹ G. Andre et E. Demoussy. Bull. Soc. Chim. Biol., vii, 806-10 (1925).

² Osterhout, W. J. V. Proc. Soc. Exper. Biol. Med., xxiv, 243-7 (1926).

Bei dieser Gelegenheit wurde der Einfluss der Diathermieströme auf den Tonus der *glatten* Muskulatur studiert. Es wurden Beobachtungen über die Dehnbarkeit der Cardia während und ausserhalb der innerlichen Diathermiebehandlung angestellt. Ferner wurde die Beeinflussung der Brech- und Würgreflexe durch den elektrischen Strom beobachtet. Die Temperaturempfindlichkeit der Speiseröhre in ihren einzelnen Abschnitten sowie des Magens konnte genau festgestellt werden. Durch Röntgenbilder konnte der Einfluss der innerlichen Diathermie auf die Funktion der Cardia sowie auf die entzündlichen Veränderungen im Oesophagus nachgewiesen werden. Die Resultate dieser Beobachtungen sollen nun an der Hand von tabellarischen Aufstellungen und belegt durch Röntgenbilder demonstriert werden.

BUELL, MARY V. (BALTIMORE). On the Origin of Inosinic Acid.

The isolation of adenine nucleotide from pig's blood and the demonstration of its occurrence in comparatively large quantities in human blood (15 to 20 mgm. per 100 cc.) and the blood of several other species, has made it seem probable from *a priori* considerations that this compound may act as the mother substance of inosinic acid of muscle. Embden's recent finding of adenine nucleotide in rabbit's muscle, together with the observation that ammonia is given off when frog muscle is stimulated and that extracts of frog and rabbit muscle bring about the deamination of added adenine nucleotide prepared from muscle, but not that prepared from yeast, lends experimental support to this view.

This problem has been studied independently for the past two years from an entirely different viewpoint. Extracts from the muscle of several species, including human muscle, have been digested with added adenine nucleotide prepared from yeast nucleic acid. If deamination occurs, the purine should be demonstrable quantitatively, after hydrolysis, as hypoxanthine; if not, as adenine. Pork, beef, and rabbit muscle were found to give rise to hypoxanthine almost quantitatively, whereas human and rat muscle were shown to have no power of deamination of adenine nucleotide prepared from yeast. The action of muscle extracts on adenine nucleotide prepared from muscle is being investigated.

BÜRGER, MAX (KIEL). Die physiologische Bedeutung der primären Insulinhyperglykämie.

Jede intravenöse Injektion von Insulin hat bei Menschen und Tieren eine vorübergehende *Vermehrung* des Blutzuckers zur Folge. Der Grad der Blutzuckervermehrung ist abhängig von dem Gefässgebiet, in welches die Insulininjektion erfolgt ist, von der Grösse der Insulindosis und von dem Glykogengehalt der Leber. *Beim Menschen* tritt 5 bis 10 Minuten nach der Injektion von $\frac{1}{2}$ Einheit Insulin Welcome pro Körper-kg in die Kubitalvene eine mittlere Steigerung des Blutzuckers von 20 Procent ein. Bei Fettleibigen und Myxödemkranken kann der Blutzucker unter gleichen Bedingungen auf 50 Procent des Ausgangswerts ansteigen. Nach direkter Injektion von 1 bis 2 Einheiten Insulin in die Pfortader oder einen ihrer Äste beträgt die *Vermehrung des Blutzuckers im Mittel von 21 Versuchen am Hund 35.3 Procent*. Wird das Insulin in die Vena jugularis injiziert und die Blutzirkulation in der Leber durch Unterbindung des Leberhilus stillgelegt, bleibt die Vermehrung des Blutzuckers im peripheren Blute aus. Die *initiale Hyperglykämie* nach *Insulininjektion* ist demnach

die wahrscheinliche Folge einer Glykogenausschüttung aus der Leber. Diese These wird durch laufende alle 10 Minuten wiederholte Glykogenbestimmungen in der Leber des Hundes mit Hilfe einer besonderen Methodik erwiesen. Das Lebergewebe wird mit einer Hohlstanze in der Monge von 0,5-1g entnommen und die Wunde übernäht, wodurch grössere Blutungen sicher vermieden werden. Es zeigt sich dabei, dass die Leber nach *Insulininjektion* in die *Pfortader regelmässig an Glykogen verarmt*. Diese Glykogenverarmung ist umso grösser, je höher der Blutzucker nach der Insulininjektion ansteigt. Die Verluste können bei intraportaler Injektion von beispielsweise 2 Einheiten Insulin pro Körper-Kg bei einem 17,5 kg schweren Hund bis zu 59 Procent des Ausgangswerts betragen. Die absoluten Glykogenverluste sind umso grösser, je höher der Ausgangswert des Leberglykogens liegt. Dieser schwankt bei gleichmässig mit Reis und Fleischextrakt ernährten Hunden zwischen 10,9 und 0,39 Procent Glykogen der frischen Substanz. Auch beim einzelnen Tier schwankt der Glykogengehalt der Leber von Lappen zu Lappen in geringem Umfange. Frühere Untersuchungen haben gezeigt, dass die Insulininjektion nach Abklemmung der Iliacae und Subclaviae keine wesentliche Hypoglykämie zustandekommen lässt; wohl aber kommt es nach Ausschaltung der Muskulatur aus dem Kreislauf zu einer Vermehrung des Blutzuckers. Auch nach Exstirpation beider Nebennieren hat die intravenöse Insulininjektion eine deutliche primäre Hyperglykämie zur Folge. Aus allen diesen Beobachtungen wird folgendes geschlossen: *Das Insulin steigert den Kohlehydratumsatz in der Leber und fördert den Kohlehydratumsatz und Verbrauch in der Muskulatur.*

BURGET, G. E. and KARL MARTZLOFF (PORTLAND, OREGON). **A Study of the Closed Loop of Jejunum.**

Because of the limited period that animals have survived a high closed intestinal loop the symptom complex reported in the literature is complicated with the effects of absorption of toxins and peritonitis. A section of the jejunum 12 to 14 cm. long with its mesenteric vessels intact was closed by inversion of the ends and then attached to the anterior abdominal wall. Two stitches were placed in the skin to indicate the point of attachment of the loop. The continuity of the gastrointestinal tract was reestablished by an end to end anastomosis. The loop was tapped with a hypodermic needle at intervals of 48 hours for the first few days after which the intervals were longer. The pressure within the loop was thus kept down and good circulation permitted; by this means a normal mucosa is maintained. When no complications arise as the result of faulty experimental technic, the clinical symptoms following the operation resemble closely those of an animal that has undergone only a simple intestinal anastomosis. Results indicate that 1, toxic products of the loop are not absorbed; 2, after 10 to 14 days the material either loses much of its toxicity or an immunity is developed or both factors play a part such that rupture of the loop may not produce critical symptoms.

BURK, NORVAL F. and DAVID M. GREENBERG (BERKELEY). **The Physical Chemistry of the Proteins in Non-Aqueous and Mixed Solvents. I. The State of Aggregation of Certain Proteins in Urea-Water Solution.**

The use of solvents other than water, that are capable of dissolving pro-

teins without entering into chemical combination with them, in contrast to the usual mode of procedure, by the addition of small amounts of acid or alkali, makes it possible to investigate the properties of the proteins in one of their most important states—the isoelectric state.

In the present investigation, one such property, the osmotic pressure was measured chiefly, making use of a 6.60 molal urea solution as solvent. The main objectives in mind were: 1, to develop a method for the determination of molecular weights of proteins that are not soluble in water in the isoelectric state, and 2, to determine whether proteins are capable of undergoing a change in their state of aggregation with a change of solvent.

From the osmotic pressure measurements in urea solution the following values for the molecular weights were obtained: casein, 33,600; edestin, 49,000; hemoglobin, 34,500 and egg albumin, 35,900. Measurements made in aqueous buffered solutions upon the water soluble proteins, hemoglobin and egg albumin, gave values of 69,000 and 36,000 respectively. The values obtained in aqueous solution are in agreement with the results obtained by other investigators by osmotic pressure measurements and by the ultra-centrifuge method.

A change of solvent was found to cause a change in the state of aggregation of hemoglobin. Dissolved in urea solution, hemoglobin was found to have a molecular weight of 34,500 as compared to the value of 68,000 when dissolved in water. The splitting of the hemoglobin aggregate into two smaller units was found to be accompanied by a denaturation of the protein. Egg albumin was found to have the same molecular weight when dissolved in a urea solution as when dissolved in water. The state of aggregation of hemoglobin was found to be the same in a glycerine solution as in aqueous solution.

BUSINCO, OTTAVIO (CAGLIARI). Sulla distribuzione degli emboli nella circolazione polmonare dimostrata radiograficamente.

Da una serie di esperienze praticate sui canii iniettando pochi cc. di una sospensione oleosa di bismuto nelle vene periferiche, risulta che la distribuzione del materiale opaco nei polmoni varia a seconda della posizione tenuta dall'animale. La prima localizzazione degli emboli si osserva nelle basi polmonari, prevalentemente a destra, solo in seguito essi si distribuiscono nel rimanente campo polmonare, bilateralmente.

BÜTTNER, H. E. (WÜRZBURG). Sympaticuswirkungen auf die Muskulatur.

Ausgehend von der Beobachtung von Hoffmann und Magnus-Alsleben, daß nach Durchschneidung der rami comm. beim Frosch eine Methylenblauinjektion die sympathektomierte Seite stärker färbt, als die Kontrollseite, haben wir in der Med. Poliklinik Würzburg eine Reihe von Sympaticuswirkungen studiert.

Bisher fanden wir nach Sympathektomie: Die Arteriolen und Capillaren sind erweitert, die Permeabilität der Letzteren nimmt zu. An Stoffwechselstörungen fanden wir: Glykogen, Milchsäure, Ammoniak vermehrt, die Bildung anorganischen Phosphors vermindert. Die Chronaxie und Refraktärphase war unverändert, ein leichteres Eintreten der Ermüdung ist wahrscheinlich. Der Verkürzungsrückstand (Tiegelsche Kontraktur) ist vergrößert. Bei Untersuchungen am Menschen sahen

wir nur selten einen stärkeren Verkürzungsrückstand (deutlich nur bei sogenannten Vagotonikern). Dieser ließ sich durch Atropin beseitigen, durch Pilocarpin hervorrufen bzw. verstärken. Die Tiegelsche Kontraktur steht demnach unter dem Einfluß des veget. Nervensystems und hat auch Beziehungen zur Ermüdung. Erschöpfungskurven (Abfallen der Kurve während des Reizes) beobachteten wir bei Gesunden nur nach erschöpfender Arbeit, bei Herzkranken dagegen häufig. Diese erschöpfungskurven können durch Massage (Zirkulationsverbesserung, Capillarisation) manchmal aufgehoben werden, die veget. regulierte Tiegelsche Kontraktur bleibt hierdurch unbeeinflusst, kann sich unter Arbeit sogar gelegentlich verstärken.

Klin. Wochenschr., 1928, 737.

Biochem. Zeitschr., 1928, cxcviii, 478.

Pflüger's Arch., 221, S. 93, 1928.

Klin. Wochenschr., 1929, 601.

CAFFIER, P. (BERLIN). **Die Rolle des menschlichen Uterus als mesodermales Verdauungsorgan. (Experimentelle Studien.)**

Die Verdauung ist im allgemeinen ein Reservat der vom Entoderm abstammenden Organe. Dass auch ein sehr wahrscheinlich mesodermales Organ wie die Milz unter bestimmten Umständen starke proteolytische Valenzen besitzt, konnte Rössle auf dem vorjährigen Deutschen Pathologenkongress zeigen. Ich selbst habe den menschlichen Uterus in dieser Beziehung studiert und dabei parallel zwei Methoden angewandt. Mir war bei *Explantations* versuchen mit menschlicher Uterusschleimhaut ein differentes proteolytisches Verhalten der Schleimhäute verschiedener Phasen aufgefallen. Ich habe daraufhin diese Befunde mit der von Müller und Jochmann angegebenen *Serum-Platten-Methode* kontrolliert und bin zu übereinstimmenden Ergebnissen gekommen, die frühere Untersuchungen von Halban, Frankl und Aschner bestätigen und erweitern.

Die drüsigen Bestandteile der Uterusschleimhaut produzieren ein proteolytisch wirksames Ferment, dessen Valenzen in praemenstrueller (praegravider) Schleimhaut am stärksten sind. In postmenstruellen Schleimhäuten ist es bestenfalls in Spuren wirksam, während Intervall-Schleimhaut in ihrem Gehalt an Trypsin wechselt. Sowohl das secernierende Drüsenepithel an sich als auch der secernierte Uterusschleim sind proteolytisch aktiv; in gleicher Weise verhält sich das Menstrualblut. Unter pathologischen Verhältnissen (glanduläre Hyperplasie) kann die wirksame Fermentquantität gleich hoch wie in praegravider Schleimhaut sein. Ein übergeordnetes regulatorisches Zentrum (Primat der Eizelle) bleibt anzunehmen, weil die Schleimhäute Neugeborener und jugendlicher Individuen vor der Menarche keine proteolytische Fähigkeit entfalten, ebenso wie diese den atrophischen Schleimhäuten postklimakterischer Personen fehlt. Der Glykogengehalt der Schleimhäute spielt bei der verdauenden Funktion keine Rolle. Zuckerlösungen, Ovarialhormon, Liquor folliculi, Zysteninhalte, Spermien, Ovula ohne Befruchtung, Tubenschleimhaut, Muskulatur und Blut sind frei von dem proteolytischen Ferment. Das Wirkungsoptimum des letzteren liegt *in vitro* bei Temperaturen um 50° Celsius, bei 80° wird es zerstört. Röntgenbestrahlung und Trocknung der Endometriumsubstanz bei optimalen Temperaturen vermindert die beschriebene Wirkung nicht.

Die Aufgaben dieses proteolytischen Fermentes sind in verschiedenen Richtungen zu suchen: Physiologischer Weise dürfte die unmittelbare Auslösung der Menstruationsblutung bei Vorhandensein einer als Aktivator wirksamen Hyperämie auf ihr Konto zu setzen sein. Die Ungerinnbarkeit des Menstrualblutes betrachten wir als eine Folge dieser Fermentbeimengung. Auch für die Quellung der Stromaelemente in der praegraviden Phase und für die schliessliche Ausbildung der Decidua bei eintretender Gravidität glauben wir das Ferment verantwortlich machen zu müssen. In den Wechselbeziehungen zwischen befruchtetem Ei und Mutterboden spielt es zweifellos eine ausschlaggebende Rolle. Sein Einfluss auf die Spermien (mögliche Zusammenhänge mit Sperma-Resorption und-Immunität) wird noch untersucht.

CAMPOS, C. M. and F. M. CAMPOS (S. PAULO). **Effects of the Toad's Poison upon the Chronaxie of the Toad's Nerve-Muscle Preparation.**

In a previous paper Campos and Santos had shown that the toad's poison (*Bufo marinus*), either injected or applied directly over the gastrocnemius produced as increase in its contracting power, a decrease of the latent period and of the total length of the isotonic curve. A very striking increase of the capacity for prolonged work was obtained. In order to explain these effects the authors studied the chronaxie of the preparation before and after the action of the poison. Boullite apparatus was used, with discharges of a condenser and Lapicque's non-polarisable electrodes, with resistance of 7,000 ohms. The poison was taken from the parotid glands and dissolved in distilled water (0.88 mgm. per cc.). Sixteen experiments were performed.

1st series. Determination of the chronaxie of both sides, before and after application of the poison. The chronaxie expressed in capacity (microfarads) was obtained between 0.037-0.067. The poison always produced a great reduction of it.

2nd series. Action of the poison on the fatigued preparation. The poison when applied to the nerve succeeded in increasing the depressed excitability observed after work.

3rd series. Action of the poison on the chronaxie was heightened by application of lactic acid. The poison brought back the chronaxie value.

Conclusion. Toad's poison decreases the chronaxie of the normal and of the fatigued nerve-muscle preparation. So it acts as adrenin, from some points of view.

CAMPOS, C. M. and F. M. CAMPOS (S. PAULO). **Presence of Sensory Fibers in the Inferior Laryngeal Nerve Trunk.**

Seven experiments were made in dogs of medium size, using morphine and chloroform as anesthetics.

In 4 experiments both nerves were stimulated by tetanizing currents, at different times. Blood pressure and respiration were recorded. In most cases increase of the blood pressure and stoppage of respiratory movements were observed. These results were gotten by the stimulation of the central end, also, and almost nothing when the electrodes were applied in the peripheral end.

Section of the superior laryngeal nerve, either of one or both sides, done three or four weeks before, did not change the final results.

Conclusion. The authors believe that their experiments show the presence of fibers running towards the central nervous system. These fibers do not belong to the superior laryngeal nerve and predominate in the inferior laryngeal nerve of the right side.

CANNON, W. B. (BOSTON). **Animals Surviving Complete Exclusion of the Sympathetic Nerve Impulses. (Demonstration)**

CARIDROIT, F. (PARIS). **L'Évolution de la gonade droite de la poule domestique après ovariectomie; ses conséquences physiologiques.**

La poule domestique normale possède un seul ovaire situé dans la partie gauche de l'abdomen. L'ablation totale de l'ovaire, réalisée depuis longtemps par Pézard et par Goodale, a pour effet de faire de la Poule un animal neutre avec plumage de coq, petite crête, ergots. Cette *forme neutre* est commune aux deux sexes.

Des expériences récentes ont montré que la chaponne ne reste souvent pas neutre très longtemps. La gonade droite, arrêtée dans son évolution depuis la seconde semaine de la vie embryonnaire et restée à cet état rudimentaire, se développe alors. Elle évolue en testicule et peut demeurer telle. Certains auteurs ont nié la possibilité pour les cellules spermatiques d'arriver jusqu'au stade spermatozoïde. Nous avons pu noter une fois la formation de ces éléments mâles. Les caractères sexuels secondaires sont ceux d'un mâle: plumage, ergots, crête du coq.

La destinée de l'organe rudimentaire droit n'est pas d'être toujours seulement un testicule. Une poule Leghorn dorée, ovariectomisée à 6 mois et que nous avons suivie ensuite 3 ans, a présenté les caractères mâles (plumage et crête) pendant 2 ans. La dernière année, elle a brusquement pris un plumage de poule mais elle a conservé sa crête de coq. L'autopsie révéla l'absence de toute gonade à gauche et la présence d'un ovario-testicule à droite.

Conclusion: L'ovariectomie de la poule a souvent comme conséquence le développement de la gonade droite restée embryonnaire qui devient un testicule ou, plus rarement, un ovario-testicule. L'oiseau présente dans ce dernier cas l'aspect d'un gynandromorphe vrai avec le plumage de la poule et la crête du coq si les tissus conditionnants sont en quantité suffisante.

CARPENTER, THORNE M. (BOSTON). **Modified Form of Apparatus for Analysis of Respiratory Chamber Air. (Demonstration)**

CARPENTER, THORNE M. and EDWARD L. FOX (BOSTON). **The Respiratory Exchange after Ingestion of Levulose and Dextrose, as Affected by Muscular Work.**

The respiratory exchange was measured by an open-circuit respiration apparatus for one hour continuously in the post-absorptive, sitting condition. Following a rest and immediately following the ingestion of 50 grams of dextrose and levulose, respectively, measurements continued for two and three-quarters hours in 15-minute periods, during the first hour of which muscular work was performed on a bicycle ergometer at the rate of 276 kilogrammeters per minute.

With 50 grams of dextrose the R.Q., at rest, rose 0.06 above basal during the second hour after ingestion. After levulose, the R.Q. rose 0.16 above

basal during the second quarter-hour after ingestion. When muscular work was performed without sugars, the R.Q. rose 0.05; following work, it was below the pre-work level. With ingestion of dextrose, the R.Q. rose during work 0.09, and fell gradually after work to about the pre-work value. With levulose, the quotient rose during work 0.11 and fell to 0.03 above basal one and three-quarters hours after the exercise ceased. When work was performed for one half-hour at 554 kilogrammeters per minute, with both sugars the maximum respiratory quotients were higher, the drop following exercise was greater, and the return to basal was earlier than after the more moderate work; but the return to a pre-work level was quicker with dextrose than with levulose. The results indicate that the course of the R.Q. after dextrose and levulose ingestion is somewhat the same, when work is done, as during rest but the transformations are more rapid. A steady physiological condition was reached within 15 minutes after the beginning of the lighter work, as indicated by the constancy of the percentage of carbon dioxide in the expired air, of the respiratory quotient, and of the efficiency.

CARRASCO-FORMIGUERA, R. (BARCELONA). Nitrogen Metabolism in Severe Diabetes.

Experiments of different types on laboratory animals as well as on human subjects show that the quantitative disturbance of nitrogen metabolism in severe diabetes, when existing, is a result of the primary disturbance of dextrose metabolism and may be influenced by dietary conditions and other factors independent of diabetes itself, and is neither a direct result of insulin insufficiency nor an essential feature of severe diabetes.

CATTELL, McKEEN and D. J. EDWARDS (NEW YORK). The Influence of Pressure on the Refractory Period and Rhythmicity of the Heart.

The increased activity of cardiac muscle resulting from the application of hydrostatic pressure is accompanied by a definite prolongation of the refractory period. Measurements have been made of the least interval between stimuli causing double responses in auricular and ventricular muscle of the turtle heart by means of the Lucas pendulum. The application of a pressure of 1000 pounds per square inch prolonged the refractory period on the average 5.4 per cent in seventeen ventricular preparations. In six experiments on auricular muscle subjected to a pressure of 1550 pounds, a pressure causing an increase of over 100 per cent in the tension developed, the average prolongation of the refractory period was 17 per cent. In these experiments there was fairly good agreement between the degree of stimulation of the tension and the prolongation of the refractory period. We believe that these results do not represent a specific influence on the rate of recovery but rather that the increased duration of the refractory period is a consequence of the augmented contraction, following which more time is required for restoration.

Pressures of the same order as those employed in the studies on the refractory period cause a definite but variable increase in the rate of rhythmically contracting auricular tissue and of the whole heart. The maximum shortening of the cycle time, in many experiments amounting to as much as 30 per cent, occurs immediately after the compression is applied and is greatest in those preparations having a slow initial rate.

The increased rate is not well maintained but gradually returns to the control value or even less, and on removal of the pressure is further temporarily slowed. Not infrequently there follows a short period of complete quiescence when the pressure is released. These observations on rate parallel those on tension in the rhythmically beating muscle, where there was found to be a gradual falling off in the maximum tension developed and upon removal of the pressure the tension drops below the pre-pressure value, following which there is slow recovery. This decline does not occur in quiescent preparations where the stimulating influence of pressure may be maintained for hours, so that it may be concluded that both the decline in rate and in tension are due to a secondary influence of pressure resulting from the high level of activity which leads to a rapid exhaustion of the resources of the tissue. In many preparations showing a partial sino-audicular block the application of pressure has resulted in the immediate assumption of a normal rhythm, with accompanying stimulation of rate and amplitude. Under these conditions block is re-established upon release of the pressure, or there may be complete loss of rhythmicity. In the light of the experiments showing a prolongation of the refractory period under pressure it appears probable that pressure influences the rate through a primary stimulating action on the functions controlling the rate of systolic discharge.

CERVERA, LEANDRE et F. FORNELLS-PUIG (BARCELONA). **Sur la nature chimique de l'agent cholestérogène par injection duodénale d'acide.**

Abelous et Soula ont découvert en 1920: 1° que l'injection intraduodénale d'une solution d'acide chlorhydrique provoque chez le chien une hypercholestérolémie très sensible. 2° que cette injection ne détermine pas d'hypercholestérolémie si le chien a été préalablement splénectomisé.

Nous avons vérifié ces faits et étudié le mécanisme de leur production. De nos expériences personnelles nous tirons deux conclusions: 1° la relation fonctionnelle entre la muqueuse duodénale et la pulpe splénique relève d'un mécanisme humoral. 2° Ce mécanisme est indépendant du système nerveux.

CHAMBERS, WILLIAM H. and HERBERT POLLACK (NEW YORK). **The Effect of Muscular Exercise Induced by Epinephrin upon the Metabolism of Depancreatized Dogs.**

Muscular contraction was caused in depancreatized dogs on the 3rd to the 5th post-operative day by the injection of epinephrin (0.5 mgm. per kilo). The metabolism was observed for 5 hourly periods in the respiration calorimeter and the urinary dextrose and nitrogen excretion determined. In a typical experiment the respiratory quotients from the 2nd to the 7th hour after the epinephrin were, respectively, 0.75, 0.74, 0.68, 0.60, 0.72. In this experiment the increase in the respiratory quotient of the 1st and 2nd hours (dog active) over the diabetic basal level of 0.69 was counterbalanced by the decrease in the 4th period (dog quiet). The average respiratory quotient for the 5 hours was 0.705, which closely approximates the basal level. After the first injection of epinephrin the urinary D:N ratio rose from the basal level of 2.9 to as high as 12.3 in one instance. A second injection of the hormone on the following day produced no extra sugar elimination. In all the experiments there was a close agreement

between the diabetic basal respiratory quotient and the average respiratory quotient of the total period of observation after epinephrin. This indicates that no sugar was being oxidized during this period of muscular activity in the depancreatized dog, in spite of the increased outpouring of sugar in the urine.

CHANUTIN, ALFRED and HERBERT SILVETTE (UNIVERSITY, VIRGINIA).
A Study of Creatine Metabolism During Partial and Complete Nephrectomy in the White Rat.

Previous work from this laboratory has shown that creatine feeding is accompanied by a rise in the creatine content of muscle, liver, and blood. An attempt has been made in this study to duplicate these experiments indirectly by causing an accumulation of creatine in the blood stream, and if possible in other tissues, by means of complete and partial nephrectomy.

The first series of experiments involved a study of a large number of control rats subjected to laparotomy, and of completely nephrectomized rats, both starved two and three days after the operative procedure. At the end of this period of fasting, the rats were killed and the tissues analyzed. The liver creatine, blood creatine, and blood creatinine of the control animals remained normal; the muscle creatine averaged 0.507 per cent as a result of the fasting. The nephrectomized animals displayed a marked increase in blood creatine and creatinine, the average for the creatine being 3.8 times that for the normal, and that of the creatinine, 5.9 times the normal. Under these conditions of a creatine and creatinine plethora in the blood, one might expect a marked deposition of both these materials in the tissues. However, it was found that the increase in the muscle was relatively small (0.538 per cent as contrasted with the control figure, 0.507 per cent). The liver creatine was increased about 300 per cent above the normal figure. As was to be expected, the total solids of the muscle of the nephrectomized animals were very definitely lowered. This factor was taken into consideration in calculating the creatine content of the muscle.

Another series of animals was nephrectomized after a period of creatine feeding. At the time of operation it was found that the stomach was always distended with this creatine food mixture. The experiment was controlled by a study of the tissues of normal animals after creatine ingestion, and after control laparotomy followed by fasting. The most striking result was the tremendous increase in blood creatine (59.2 mgm./100 cc. blood), and in blood creatinine (16.5 mgm./100 cc.). In addition, the muscle creatine was increased to 0.561 per cent, and the liver creatine to 0.264 per cent.

Partially nephrectomized animals in which over one and one-half kidneys were removed showed very little change in creatine content from the normal, if the animals were allowed time to compensate for the kidney loss.

The results of these experiments can be interpreted in many ways. The limited capacity of the muscle for creatine storage under the conditions cited above may possibly confirm the idea that creatine is a waste product in the blood stream. Furthermore, we believe that our evidence points to a conversion of creatine to creatinine. It is rather difficult to interpret the rôle of the liver in creatine metabolism. Either the liver serves as a temporary storehouse for creatine, or it takes an active part in the metabolism of this material.

CHAUCHARD, A. et B. CHAUCHARD (PARIS). **L'anesthésie générale par compression du cerveau.**

L'introduction d'anesthésiques chimiques dans l'organisme fait intervenir dans les problèmes physiologiques un facteur dont il n'est pas facile de faire la part. En particulier, dans les recherches quantitatives sur l'excitabilité, il est préférable d'éviter de recourir à ces agents. Et cependant, on ne saurait proposer de se livrer sur des animaux éveillés à des opérations souvent douloureuses. Or, on sait que la compression du cerveau entraîne des phénomènes de torpeur qui peuvent aller jusqu'à l'anesthésie complète. Ce moyen avait été proposé, il y a déjà longtemps, comme mode de narcose chez le chien, mais il n'était jamais entré dans la pratique, faute, sans doute, d'en avoir exactement fixé la technique, et aussi par suite de difficultés résultant du défaut d'instrumentation appropriée. Nous avons étudié la question et voici comment nous l'avons résolue. La tête de l'animal étant solidement fixée par un appareil de contention spécial, on fait, dans le sens sagittal, de la région occipitale à la région frontale et sur une largeur de deux centimètres, une anesthésie locale par réfrigération (air liquide, neige carbonique, etc.); on incise la peau; on pratique, au vertex, un orifice de 1 cm. 5 environ de diamètre, en utilisant un trépan électrique à débrayage automatique de manière à éviter toute lésion de la dure-mère. On introduit alors, entre cette membrane et la paroi crânienne, un corps compressible, tel qu'un fragment d'éponge; on gradue avec soin la compression du cerveau avec un bouchon que l'on introduit dans l'orifice. En cas de rigidité des membres ou d'arrêt respiratoire, il faut décompresser rapidement. L'opération est complètement indolore, du fait de l'anesthésie locale elle est rapide, la trépanation électrique s'effectuant en 5 ou 6 secondes; l'anesthésie générale elle-même ne demande, quand elle est bien réglée, que 3 ou 4 minutes. Nous l'avons appliquée à diverses espèces animales, chien, lapin, grenouille. Par ailleurs nous avons montré qu'elle est liée à une anémie partielle des centres cérébraux.

CHAUCHARD, A. et B. CHAUCHARD (PARIS). **Analyse expérimentale de l'excitabilité du système itératif pneumogastrique inhibiteur cardiaque. (Démonstration)**

Il y a un certain nombre de nerfs dont l'excitation n'est suivie d'aucune réponse de l'élément innervé si on se borne à porter sur eux un stimulus isolé si intense soit-il. Ainsi en est-il du pneumogastrique, des vaso-moteurs, du splanchnique et, en général des nerfs du domaine sympathique et parasympathique. Seule la répétition du stimulus est efficace; c'est pour cela qu'ils ont été appelés itératifs par L. Lapicque qui a imaginé un circuit électrique grâce auquel on peut en analyser les divers éléments de l'excitabilité. Ce circuit comprend une source de courant continu d'intensité réglable qui, rythmiquement, charge des condensateurs de capacité graduée, et les décharge sur le nerf supporté par des électrodes impolarisables. Ce dispositif permet de mesurer la chronaxie, constante de temps caractérisant l'excitabilité du nerf, et de déterminer, en faisant varier le nombre des excitations et leur intervalle, les lois de sommation, caractéristiques de l'excitabilité de l'élément innervé.

CHEMIN, E. (PARIS). **Les mouvements amiboïdes des spores de *Bonnemaisonia asparagoides* Ag.**

Les mouvements des spores ont été observés chez les Bangiacées par Janczewski (1873), Goebel (1878), Berthold (1882), Joffé (1896) et plus récemment par Kylin (1921). Chez les véritables *Floridées*, ces mouvements n'avaient été signalés que dans une seule espèce, *Helminthora divaricata*, par Thuret et Bornet (1867). Je les ai observés et décrits dans deux espèces du genre *Scinaia* (C. R. de la Soc. de Biol. 1927. t. xevii, p. 1677).

Les spores de *Bonnemaisonia asparagoides*, pendant plusieurs heures après leur sortie du cystocarpe montrent des déformations continuelles. D'une forme ovale elles passent à des formes lobées, les lobes apparaissant tantôt d'un côté, tantôt de l'autre. Ces changements sont assez rapides, et, dans les dessins à la chambre claire, il faut se hâter pour en préciser les contours. La fig. 1 représente douze formes successives d'une même spore prises chacune à vingt secondes d'intervalle.

Les déformations s'accompagnent d'un déplacement. Il est faible, mais cependant appréciable. On s'en assure en se servant d'un oculaire contenant un diaphragme quadrillé, et en repérant la place d'une spore par rapport à un point déterminé du réseau. La fig. 2 représente les emplacements successifs à cinq minutes d'intervalle, d'une même spore; elle s'est déplacée vers le bas et à droite, puis vers le haut, de là elle est passée à gauche pour revenir sensiblement à son point de départ après unedemi-heure, ayant décrit une courbe fermée. On peut évaluer à 350 μ environ l'espace parcouru pendant ce temps.

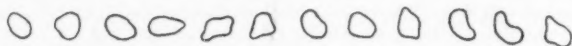


Fig. 1

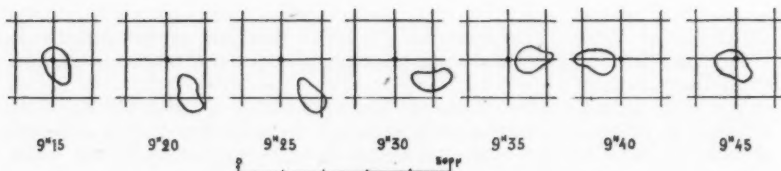


Fig. 2

On peut donc assimiler les mouvements des spores de *Bonnemaisonia* à ceux des *Amibes*, et les considérer comme une conséquence des échanges osmotiques entre elles et le milieu ambiant.

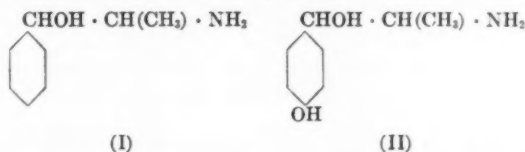
CHEN, K. K. and H. JENSEN (BALTIMORE). **The Action of Crystalline Bodies Isolated from Ch'an Su, the Dried Venom of the Chinese Toad.**

A preliminary report of this work was published in Proc. Soc. Exper. Biol. Med., 1928-1929, xxvi, 378, and in Journ. Amer. Pharm. Assoc., 1929, xviii, 244. Four active principles have been studied pharmacologically. 1. *Cholesterol* shows spectroscopically an ergosterol content of

2 parts per thousand. An irradiated sample produces a 3 plus or 4 plus healing of rats' rickets by a dose of 3 mgm. 2. *Epinephrin*, aside from the correct chemical analysis, has the same pressor activity as that from *Bufo aqua* isolated by Abel, and that from adrenal glands prepared commercially. 3. *Bufagin* is poisonous to amphibian and mammalian hearts, producing systolic standstill. 4. A *N*-containing compound is more poisonous to the heart than bufagin.

CHEN, K. K., CHANG-KENG WU and HENRIKSEN ERLE (BALTIMORE).
Relationship between the Pharmacological Action and the Chemical Constitution and Configuration. Ephedrine Series.

A preliminary report of this work was published in Proc. Soc. Exper. Biol. Med., 1928-1929, xxvi, 348. In view of the fact that primary amines are more powerful than secondary amines and that the introduction of a phenolic OH group at para-position intensifies the action, the following two compounds were compared with ephedrine.



Both compounds were synthesized by Dr. W. H. Hartung. Compound (I) was found to possess a stronger pressor action than *dl*-ephedrine, to have a mean lethal dose of 70 mgm. per kilo in albino rabbits injected intravenously, and to raise systolic blood pressure in men when given by mouth. Compound (II) has a stronger pressor action than both *dl*- and *l*-ephedrine. Its mean lethal dose intravenously in albino rabbits is 130 mgm. per kilo. No demonstrable rise of blood pressure has yet been observed in men by oral administration. A detailed account of this work appears in Journ. Pharm. Exper. Therap., 1929, July number.

CHISTONI, ALFREDO (PARMA). **Sopra i principi attivi degli estratti dei gangli linfatici.**

Come è noto, gli estratti linfatici, studiati biologicamente, hanno dimostrato avere un'azione antagonista a quella dell'adrenalina e per quanto riguarda la natura dei principi attivi molto si è discusso. Qualcuno pensa si tratti di istamina, altri più recentemente ammette che il principio attivo non sia altro che la colina. L'A., dopo avere preparato un estratto di gangli linfatici mesenterici, appartenenti a giovani bovini, e che alla prova biologica si è dimostrato molto attivo, lo ha diviso in varie porzioni sottoponendole poi all'azione di reattivi precipitanti per privarle di vari gruppi di sostanze. Si è potuto osservare che i principi attivi non vengono precipitati mediante acido acetico a caldo, non vengono estratti da l'etere o dal cloroformio nelle soluzioni acide od alcaline, non vengono estratti mediante alcool assoluto, ciò che dimostra non trattarsi di colina, la quale, come si sa, viene tolta mediante alcool assoluto dall'estratto linfatico concentrato nel vuoto ed a temperatura di circa 40°C. L'acido fosfowolframico, che precipita alcaloidi, buona parte di peptoni, la istamina, la arginina, la lisina, la cistina, la istidina, la fenilalalina, non precipita

principi attivi i quali rimangono nel filtrato e si possono dimostrare biologicamente. Anche l'acido fosfomolibdico, il quale precipitata ancor più completamente le sostanze precipitate dall'acido fosfowolframico, non influenza i principi attivi degli estratti linfatici. Quindi con tutta probabilità detti principi attivi entrano a far parte di quella piccola porzione di sostanze azotate (azoto mmgr. 2.8%) dell'estratto che non vengono tolte mediante la completa precipitazione con acido fosfomolibdico.

CHOU, TSAN-QUO (PEPING). **The Alkaloids of Chinese Corydalis Ambigua, Cham. Et Seh (Yen-Hu-So).**

From the tubers of Chinese Corydalis (Yen-Hu-So), 9 alkaloids—Corydalis A to I, have been isolated. The following table gives a summary of these alkaloids:

NAME	MOLECULAR FORMULA	M.P.	SPECIFIC ROTATION	IDENTIFICATION
Corydalis A.....	$C_{22}H_{27}O_4N$	135°	+295°	Corydaline
Corydalis B.....	$C_{26}H_{33}O_4N$	148-149°	0°	Protopine (?)
Corydalis C.....	$C_{26}H_{33}O_4N$	201°	0°	
Corydalis D.....	$C_{18}H_{16}O_4N$ or $C_{18}H_{17}O_4N$	204°	-295°	
Corydalis E.....	$C_{26}H_{33}O_4N$	219°		Corybulbine
Corydalis F.....		237°	-250°	
Corydalis G.....		237°	+300°	
Corydalis H (HBr salt).....		235°	0°	
Corydalis I.....		104°	+112.5°	

Preliminary physiological tests of some of these alkaloids by Doctors Chu and Pak showed that Corydalis B has narcotic and local anaesthetic properties and a cardiac augmentor action. Corydalis C is apparently a cerebral stimulant and Corydalis I a nervous depressant.

CIACCIO, C. (MESSINA). **Distribuzione dei lipidi nei costituenti morfologici della cellula.**

I lipidi considerati come costituenti primari ed essenziali della cellula-istolipidi-solo in parte sono dimostrabili con processi istochimici e certamente in proporzioni tali da non giustificare la considerevole quantità estraibile coi solventi. Tale discordanza rilevata già da tempo, potrebbe essere riferita a due fattori:

1. O che gliistolipidi preesistono in gran parte in uno stato speciale chimico-fisico in modo da essere facilmente allontanati coi processi di tecnica microscopica ordinariamente adoperati;

2. O che gliistolipidi si trovano in uno stato tale da non essere dimostrabili coi processi in uso per la dimostrazione della sostanze grasse.

Recentemente sono riuscito con alcuni procedimenti a mettere in evidenza coi comuni coloranti dei grassi e rispettivamente coi metodi Ciaccio e Smith-Dietrich gliistolipidi non dimostrabili direttamente.

Tali processi di lipofanerosi, conservando sufficientemente e spesso molto bene la morfologia dei costituenti cellulari, permettono di stabilire fino ad un certo punto la distribuzione endocellulare degliistolipidi.

Ciò premesso, bisogna distinguere due specie principali diistolipidi e cioè:

1. Istolipidi direttamente dimostrabili coi metodi in uso per la dimostrazione delle sostanze grasse;

2. Istolipidi dimostrabili con questi metodi dopo azione di agenti lipofanogeni.

I lipidi della prima specie entrano nella costituzione: del condrioma, dell'idiozoma e dei corpi periidiazomici delle cellule sessuali, dell'endoplasma di alcune cellule e di granulazioni speciali, di alcune membrane.

Riguardo ai lipidi della 2^a specie, ho ottenuto i seguenti risultati:

1. Presenza costante di essi ed in quantità considerevole in un sistema speciale del citoplasma connesso con immagini morfologiche, che tuttora formano oggetto di viva discussione—apparato di Golgi, vacuoma—e per il quale ho proposto il termine di ergoplasma;

2. Nel condrioma e nell'endoplasma pare che oltre a lipidi della prima specie ne se trovano anche della seconda;

3. Non è possibile anche coi mezzi più energici di lipofanerosi rilevare presenza di lipidi nella zona periferica del citoplasma e nella cromatina nucleare;

4. In condizioni abnormi questa categoria di lipidi può essere dimostrata direttamente coi metodi in uso.

Da numerose ricerche risulta che l'ergoplasma ricco di istolipidi ha una grande importanza nel metabolismo cellulare.

CLARK, ELIOT R. and J. C. SANDISON (PHILADELPHIA). **Methods for the Microscopic Study of Living Cells and Tissues in the Tail of the Amphibian Larva and in a Transparent Chamber Introduced into the Rabbit's Ear. (Demonstration)**

By the two methods demonstrated it is possible to watch the morphological changes which occur in individual cells during normal growth and activity as well as under a wide variety of experimental conditions. The method for the study of the tail of the amphibian larva is an adaptation of older methods for the study of this classical object which enables one to make observations of the same cells extending over several weeks. The "rabbit's ear" method represents the results of an endeavor to make available a field for similar studies in a mammal. A double-walled transparent chamber is introduced into the ear, and the growth and activity of the cellular elements of a variety of tissues may be studied with the highest powers of the microscope.

CLARK, JANET HOWELL (BALTIMORE). **A Study of Tendons, Bones, and Other Forms of Connective Tissue by Means of X-Ray Diffraction Patterns.**

A narrow beam of monochromatic x-rays, on passing through a substance, produces characteristic diffraction patterns as follows: a single crystal gives isolated spots; a crystal powder or unoriented microcrystals, sharp rings; oriented microcrystals, a fibre pattern of arcs or spots; amorphous material, ill-defined zones; liquid crystals, broad hazy rings. Collagen in fresh unstretched tendons exists in amorphous condition with molecular spacing of 6.2 A. U. Fresh stretched tendon gives two spots on the second order zone of the diffraction pattern showing the presence of oriented crystallites with molecular spacing of 3.1 A. U. Dried tendon shows unoriented crystallites with spacing 2.9 A. U. Collagen in costal

cartilage is amorphous with a spacing of 6.2 A. U. Bone, both fresh and dried, shows a sharp crystal ring on the edge of the second order zone given by cartilage. This means that solid crystallites of collagen are present in bone with a spacing of 3.1 A. U. These collagen crystallites are unoriented but the bone diffraction pattern also shows arcs indicating oriented crystals, probably also of organic origin, with a spacing of 3.8 A. U. There is no evidence of spots characteristic of crystalline calcium salts, as in egg-shell patterns, so that the calcium salts in bone are probably amorphous and the crystallites are of organic origin. Decalcified bone gives an amorphous pattern as the process of decalcification decrystallizes the collagen. Slices from rat sarcoma I give a zone roughly identical with fibrous collagen but condensed into a broad hazy ring indicating a greater molecular orientation and a liquid crystal rather than amorphous condition.

Densitometer curves from these diffraction patterns show the change in physical character of the collagen in different forms of connective tissue.

COHN, EDWIN J., THOMAS L. McMECKIN and GEORGE R. MINOT (BOSTON). **The Nature of the Material Effective in Pernicious Anemia.**
III.

The discovery that a diet containing liver was effective in blood regeneration in pernicious anemia,¹ opened to investigation the nature of the active substance. That it was soluble in water, and in alcohol-water mixtures, has been previously reported.² Isoelectric precipitation and heat coagulation freed the extracts of protein; ether of lipoids; and lead acetate of carbohydrates. Since the active principle was neither protein, carbohydrate, nor lipid, was precipitated by mercuric acetate, and by phosphotungstic acid, it appeared to be a nitrogenous base or polypeptide.³

Although but slightly soluble in 95 per cent alcohol, the active principle has been dissolved in it following regeneration of the precipitated phosphotungstates. The undissolved proteoses, peptones, and polypeptides were inactive. The active solution gave no precipitate with trichloroacetic acid or tungstic oxide, no increase in amino nitrogen upon hydrolysis, and no biuret test, indicating that the active principle was not a peptide, but rather a nitrogenous base.

Upon concentrating this alcoholic solution, the active principle precipitated whereas depressor substances remained largely dissolved. The precipitate which was active in but small amount has been successfully injected intravenously.

The fraction employed intravenously consists largely of nitrogenous bases. Purine bases have been removed, and no material is precipitated by flavianic acid from neutral solution. Silver precipitable material may be removed earlier in the process,^{3,4} but in highly purified solutions heavy metals appear to destroy activity.

¹ G. R. Minot and W. P. Murphy. *Journ. Amer. Med. Assoc.*, 1926, lxxxvii, 470; 1927, lxxxix, 759.

² E. J. Cohn, G. R. Minot, J. F. Fulton, H. F. Ulrichs, F. C. Sargent, J. H. Weare and W. P. Murphy. *Journ. Biol. Chem.*, 1927, lxxiv, lxix.

³ E. J. Cohn, G. R. Minot, G. A. Alles and W. T. Salter. *Journ. Biol. Chem.*, 1928, lxxvii, 325.

⁴ R. West and E. G. Nichols. *Journ. Amer. Med. Assoc.*, 1928, xci, 867.

The purest active fraction dissolves in water, alcohol, phenol, glycerol, formamide, and acetic acid. Combined with acetic acid, it dissolved in such organic solvents as chloroform and carbon tetrachloride. A fraction is extracted by pyridine or by butyl alcohol. The color reactions of certain specific groups are being followed, as are acid and basic dissociation constants in the further separations that are being made in the attempt to isolate the active principle.

COOPER, S. (OXFORD). **Photographs of Isometric Maximal Motor Contractions. (Demonstration)**

CORI, C. F. and G. T. CORI (BUFFALO). **The Fate of Glucose and Other Sugars (Mannose, Fructose, Dihydroxyacetone) in Eviscerated Animals.**

A carbohydrate balance was made on eviscerated rats, consisting in a determination of the changes in free sugar, lactic acid, glycogen and respiratory metabolism following the intravenous injection of three hexoses and one triose. Evisceration alone produces a decrease in muscle glycogen and a corresponding increase in lactic acid. The respiratory quotient rises markedly, but when a correction is made for the CO_2 driven out by the lactic acid formed, it becomes evident that only fat and protein are being oxidized. Without simultaneous administration of insulin the largest part of injected sugar can be recovered from the tissues, because the eviscerated rat is unable to oxidize any of the sugars mentioned. The R.Q. and lactic acid after glucose and mannose are the same as after evisceration alone. After fructose the R.Q. is much higher, but the corrected R.Q. is in the neighborhood of 0.71. Whereas glucose and mannose are not changed to lactic acid, part of injected fructose undergoes this transformation. Glycogen formation in muscles occurs even if no insulin is injected, more glycogen being formed from glucose than from the other sugars. Since breakdown of muscle glycogen is taking place at the same time, the actual increase in muscle glycogen may not be very large. After injection of small doses of insulin, oxidation of glucose proceeds more rapidly than that of the other sugars and consequently more glucose disappears than mannose or fructose. There seems to exist a closer relationship between insulin and glucose than between insulin and the other sugars.

CORYLLOS, POLN. and G. L. BIRNBAUM (NEW YORK); YANDELL HENDERSON, H. W. HAGGARD and E. M. RADLOFF (NEW HAVEN). **The Production and Relief of Atelectasis and of Pneumonia. (Demonstration)**

In patients after surgical operations the development of the so-called massive collapse, or atelectasis, of the lung is an essential factor or stage in the development of pneumonia. Deep breathing induced by inhalation of carbon dioxide dilates the lung again. By thus overcoming atelectasis this inhalation prevents the development of pneumonia.

In medical pneumonia also bronchial obstruction develops and produces atelectasis, which in turn causes accumulation of exudate and consolidation.

The purpose of the experiments, of which the results are here reported, was to determine whether the deep breathing induced by inhalation of carbon dioxide will open up closed areas of the lungs in pneumonia, and thus prevent consolidation. In its essentials this treatment of atelectasis

and pneumonia is similar to that for the treatment of carbon monoxide asphyxia.

In the experiments dogs were narcotized with amytal, and a virulent culture of pneumococci type II was introduced through a bronchoscope into the right lung. Pneumonia generally developed, and in nearly all such cases, if not treated with inhalation of carbon dioxide, the animals died in from one to three days. If, however, soon after the development of pneumonia the animals were placed in an atmosphere of 5 to 7 per cent carbon dioxide, the collapsed and pneumonic areas of the lung cleared up to a large extent in a few hours, and many of the cases made a complete recovery.

The demonstration consists of x-ray pictures illustrating the collapse of the lung induced when an obstruction is placed in a bronchus, and the rapid redistention of the lung when the obstruction is removed and the animal placed in a chamber containing 5 to 7 per cent carbon dioxide in air. Similar x-ray pictures are exhibited of atelectasis in dogs with pneumonia, together with pictures showing the redistention of the lung induced by inhalation of carbon dioxide.

COWARD, K. H., K. M. KEY and B. G. E. MORGAN (LONDON). **Some Evidence of the Existence of a Further Factor Necessary for Growth of the Rat.**

The vitamin A-free diet in use in the laboratories of the Pharmaceutical Society of Great Britain, when supplemented with daily doses of cod liver oil up to 0.2 gram per day was found, in certain rats of known histories, to fail to promote growth to maturity. Such rats resumed rapid growth on the substitution of "light-white" casein (a B.D.H. preparation) for the vitamin-free casein in the diet, or on the addition of lettuce, wheat embryo, milk or grass (fresh or dried), beef muscle or liver or, to a lesser extent, watercress, butter, or wheat germ oil (three samples). Extra dried yeast and marmite were practically valueless. The active factor can be extracted from the "light-white" casein by hot alcohol (with partial destruction) and only slightly by cold ether (after alcohol). It is more easily extracted by hot ether from wheat embryo. The "light-white" casein retains some, but not all, of its activity after seven days' heating in thin layers in an oven at 105°C. "Crude" casein, extra agar-agar, paraffin, and salt in the drinking water are all without influence in these experiments.

"Light-white" casein contains no B₁ or B₂ vitamin but supplements a vitamin B-free diet plus excessive doses of B₁ (Peters' method of extraction) and B₂ (autoclaved marmite). "Crude" casein does not do this; the ether-extracted "light-white" casein does it to a somewhat diminished extent.

This factor is not vitamin E for (a) it is not as heat stable as vitamin E; (b) no sample of wheat-germ oil has been found to be rich in it, doses as high as 0.16 gram having given only slight response; (c) etiolated shoots (wheat) are less active than green ones; (d) a deficiency of it causes a cessation of the oestrous cycle in the rat.

CRAMER, W. (LONDON). **On the Functional Activity of the Adrenal Gland.**

The object of this communication is to demonstrate by lantern slides a

method which gives direct and conclusive evidence on the functional activity of the adrenal medulla. The methods previously available, such as changes in the blood sugar, the denervated iris, the denervated heart, etc. are indirect methods which in the hands of different observers have given results which are either contradictory, or, if not contradictory, capable of different interpretations. Direct evidence of the functional activity of an endocrine organ can be obtained only by a method involving a microscopic technique. In fact the conception of an internal secretion is at present based only on a theoretical postulate and not on visual demonstration. So many claims of an alleged secretory activity of the adrenal gland have failed to withstand critical examination that a few years ago several workers even raised the question whether the adrenal medulla ever does actively secrete adrenalin into the blood. A simple method has been worked out which renders visible by fixation in osmic acid vapour adrenalin as granules in the medullary cells of the resting adrenal. When the gland is stimulated to activity these adrenalin granules are seen to be expelled into the veins of the gland giving a clear visual demonstration of "internal secretion." In this way two new facts have been elicited which have an important bearing on the mechanism of heat regulation and on the genesis of fever.

1. Exposure to cold is a powerful stimulus to the adrenal medulla.

2. Prolonged stimulation of the gland leading to a continued adrenalin-aemia produces fever.

These findings have since been confirmed by Boothby and Sandiford (calorigenic action of adrenalin), Aub, Cannon and their collaborators. The osmic vapour method has confirmed the secretion of adrenalin in asphyxia and in ether anaesthesia, but failed to confirm the alleged secretion of adrenalin in oxygen deficiency and after insulin, which has been postulated on the basis of the indirect methods.

The method has also rendered it possible to demonstrate a correlation between medulla and cortex, and the existence in the adrenal gland of a mechanism which serves to inhibit the functional activity of the gland.

It is urged that future investigations on the functional activity of the adrenal should be controlled by this method.

CRANDALL, L. A. (CHICAGO), C. D. LEAKE (SAN FRANCISCO), A. S. LOEVENHART and C. W. MEUHLBERGER (MADISON, WISCONSIN).

The Rate of Disappearance of Glyceryl Trinitrate From the Blood Stream After Intravenous Injection.

The amount of glyceryl trinitrate in blood was determined by ether extraction, alkaline hydrolysis of the ether extract, and by application of the von Griess colorimetric reaction which depends on the formation of a pink azo-dye by sulphanilic acid and α -naphthylamine in the presence of nitrous acid. The method is quite accurate for amounts as small as 0.5 mgm. glyceryl trinitrate per liter of blood. In the range of concentration used in these experiments, this method was found to be 95 per cent accurate when applied to specimens of blood *in vitro* to which known amounts of glyceryl trinitrate had been added.

Following the intravenous injection in dogs of glyceryl trinitrate in dosages of 10 mgm. per kilo or less, the rate of disappearance from the blood stream is rapid, no significant amounts being detectable twenty minutes after injection. One minute after injection an average of only 14

per cent of the amount administered may be detected in the blood stream, the maximum recovery at this period being 28 per cent and the minimum recovery being 6 per cent. The amount detectable varies with the dosage, a smaller percentage of the quantity injected being detectable at a dosage of 5 mgm. per kilo than after an injection of 10 mgm. per kilo. The blood pressure remains below normal levels 5 to 10 minutes after no significant amounts of glyceryltrinitrate may be observed in the blood stream. The blood pressure tends to remain low for a longer time in those animals in which the rate of elimination from the blood stream is slow. Anesthesia has no effect on the rate of disappearance of glyceryl trinitrate from the blood. There is little evidence that tolerance induced by the oral administration of glyceryl trinitrate and by the inhalation of amyl nitrite has any effect on the rate of disappearance of glyceryl trinitrate from the blood stream after intravenous injection.

CROWDEN, G. P. (LONDON). The Replacement of Depleted Adrenaline in the Suprarenal Glands.

The application of external cold is a controllable method of producing exhaustion of the adrenaline store of the suprarenal glands of cats provided a marked fall in body temperature occurs and persists over a sufficient period of time. The effective stimulus is estimated in terms of degree-hours internal cold produced.

The replacement of adrenaline in innervated and in denervated glands following partial exhaustion of the glands by cold has been investigated, and the conclusion is drawn that the replacement of adrenaline may proceed without nervous control.

CROZIER, W. J. and G. PINCUS¹ (CAMBRIDGE, MASSACHUSETTS). The Geotropic Orientation of Young Rats.

Quantitative formulations of the extent of upward geotropic orientation of young rats as a function of the inclination of the surface on which creeping takes place, under standardized conditions, are of similar type but with different, characteristic values of the contained constants when several different, genetically stabilized lines are compared. The biological reality of these differences has been subjected to radical test by investigating their behavior in inheritance.

On the assumption that orientation during steady progression on a sloping surface is achieved when the tension-excitations connected with the use of the appendages on the two sides of the body are the same, within a threshold difference, the angle of the path on the surface (θ) can be taken as a measure of the total excitation. This must be regarded as involving, over appreciable intervals, 1, the total array of receptors excited, a function of the stretching force, and 2, the frequency of change in tension; the latter is to be assumed largely determined by the frequency of stepping, and should thus be proportional to the speed of movement. This speed is directly proportional to $\log \sin \alpha$ (α being the slope). Hence $\Delta\theta/\Delta \log \sin \alpha$ plotted against $\sin \alpha$ should give a picture of the distribution of effective thresholds among the available tension receptors. For the races studied this distribution can be resolved in each case into three groups. It is found that by attaching weights to the animals, these groups may be differentially modified.

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In one race (*K*) the three groups are large, in another (*A*), small. In crosses between these two lines and in the back-cross progenies there is clear evidence of the independent segregation of the factors responsible for "largeness" and "smallness" of these groups.

These considerations imply a mode of definition of a *gene* in terms of its expression as a function of some controlling, independent variable. They also indicate a procedure which may be applicable in other cases for testing the reality of quantitative formulations of conduct.

CROZIER, W. J., T. J. B. STIER and G. PINCUS¹ (CAMBRIDGE, MASSACHUSETTS). **On the Theory of "Temperature Characteristics."**

During the past several years data have been accumulated dealing with the relations between temperature and the frequencies and speeds of processes in organisms, to provide further basis for the interpretation of such relationships. In the very great majority of cases the well-known equation due to Arrhenius is accurately descriptive, and more precisely serviceable than any "simpler" empirical formula devoid of theoretic status. At certain particular temperatures, different for different activities and for different organisms, abrupt changes in these curves define what have been termed "critical temperatures." The possible specific significance of the descriptive term (temperature characteristic) in the Arrhenius formula has been tested in several ways. The fact that in general the temperature characteristics for two different activities in the same individual, observed at the same time, are not the same, points to specific meaning. In groups of genetically stabilized lines of suitable organisms (young mice) it is found that a small number of very well defined temperature characteristics is exhibited for the frequency of breathing movements as a function of body temperature, and that the values of these characteristics are sharply contrasted with those obtained for other equally stabilized but non-related strains. In fact there is sufficient evidence to assure the probability that the inheritance of these specific constants can be followed in breeding experiments.

By the treatment of a suitable organism (such as the transparent mollusk *Dendronotus*) with a drug, it has been attempted to modify the temperature characteristics for the frequency of the heart beat in the intact animal. It is found that such modification is possible, and specific. Such effects are not to be confused with those apparent in experiments designed to measure "the temperature coefficient for the action of" the drug; the effect of, for example, strychnine, or caffeine, is not merely to change the frequency of heart beat, but on the contrary to alter fundamentally the way in which the frequency of contraction is controlled by the temperature.

Given observations made with sufficient attention to manipulative detail, it is uniformly found that the variability of the rate of a biological process at a given temperature is a constant fraction of the mean frequency at that temperature, over a range of temperatures to which a single temperature characteristic applies. When a constant, adequately large, number of observations is available at each of a number of temperatures, the temperature characteristic for the standard deviation of the measured rates or frequencies is identical with that for the mean rates. Since in this way it can be shown that the variability of performance expressed as a

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percentage of the mean value is not itself a function of the temperature, it may be concluded that the physical properties of the system in which there is occurring the chemical change which determines the magnitude of a critical thermal increment are not altered in any relevant manner as a function of the temperature—and therefore that attempts to involve considerations of protoplasmic viscosity, for example, are unwarranted.

CRUICKSHANK, E. W. H. (HALIFAX). The Effect of Insulin on the Utilisation of Sugar in the Normal and Diabetic Heart.

The isolated heart lung preparation of Starling was used in these experiments, dogs were employed as subjects of the experiments, and the heart and lungs perfused with defibrinated dog's blood.

It has been shown that the isolated normal heart responds to insulin by storing glycogen provided that the blood sugar does not fall to an extremely low level. The diabetic heart, however, will not react in such a manner to injected insulin unless the blood sugar be maintained well above the normal figure.

The average figure for the utilisation of sugar by the normal isolated heart, when no sugar is added to the blood during a two hours' experiment, was 2.24 mgm. per gram of heart muscle per hour. Upon the addition of sugar to the perfusing blood the storage of glycogen and the utilisation of sugar are markedly increased.

Insulin increases sugar utilisation some threefold in the normal, while in the heart fed with sugar utilisation is increased sixfold.

Perfusion of a diabetic heart with normal blood results in a figure for sugar utilisation which averages 4 mgm. per gram of heart muscle per hour. On the other hand, the perfusion of a diabetic heart with diabetic blood, that is, with blood from a dog nine days diabetic, results in no utilisation whatsoever. It would appear that insulin is eliminated rather thoroughly from the blood in the course of six to eight days after complete pancreatectomy.

Insulin added to diabetic blood perfusing a diabetic heart increases the power of the heart to utilise sugar 7 mgm. per gram per hour, but seems to fail to effect a synthesis of glycogen. Even when insulin is added at the rate of 10 units half hourly, no glycogen synthesis is obtained. If, however, normal blood be added, the glycogen content of the heart is usually well maintained at or about the normal, and the sugar utilisation markedly increased if the blood sugar percentage be kept at or above the normal.

CULLEN, GLENN E. and IMOGENE EARLE (NASHVILLE, TENNESSEE). The Variation of Acid-Base Condition in the Individual Throughout the Day.

This study was made to determine the actual physiological variation in the acid base condition of normal individuals throughout an ordinary day. No attempt was made to control meals or exercise. Thirteen complete series on ten individuals, faculty and students, were made. Serum pH and CO_2 content, urine pH, titratable and total acidity determinations were made on samples taken in the morning before rising and at intervals thereafter until about 10 p.m.

Contrary to our expectations there is an *increase* in pH, which may be interrupted by fluctuations throughout the day. There was usually an *increase* in pH at noon. From then until 10 p.m. different individuals

fluctuate considerably but in general at 6 p.m. the pH is higher than in the morning. The pH, between 8:30 and 10 p.m. was from 0.01 to 0.08 pH more alkaline than before rising. There was no consistent effect due to meals. These results indicate the necessity of using basal or standard conditions for comparing results in doing pH determinations, and also suggest that the effect on pH and CO₂ content of HCl secretion in the stomach is not a constant.

CUNNINGHAM, R. S., E. H. TOMPKINS, J. W. BEARD, L. A. BEARD and J. T. GEIGER (NASHVILLE, TENNESSEE). **The Maturation, Emigration and Distribution of the White Blood Cells.**

It has been shown that the intravenous injection of large amounts of *B. typhosus* or *B. coli* will produce a massive leucocytosis with almost complete depletion of the myeloid elements of the marrow. Similar results have been obtained with certain derivatives of nucleic acid. We have recently found that when such a leucocytosis is induced in tuberculous animals, the monocytes increase in the same or even greater proportion than the granulocytes (in normal animals the monocytes increase very slightly following such an injection). In this experiment, there are certainly two factors involved, the one increasing the rate of production of monocytes, and the other increasing the rate of their emigration into the circulation.

It has long been known that certain organic substances, *e.g.*, proteins and the higher derivatives of proteins, will produce an acute leucopenia. We have found that this can also be done by certain inorganic salts, *e.g.*, disodium hydrogen phosphate. This reaction, since it is produced by substances of such divergent chemical nature, is probably the result of some physico-chemical change (such as surface reactions, etc.) in the blood cells, in the endothelium of the reservoirs, or in both.

This group of observations, as a whole, suggests that there are three distinct phases in the formation and distribution of the leucocytes; namely, maturation, emigration and distribution, and that there is a special group of factors concerned in the control of each of these phases.

CUSHING, HARVEY and HAROLD M. TEEL (BOSTON). **Concerning the Hypophyseal (Pars Distalis) Hormones for Growth and for Reproductive Processes.**

Experiments with the injection of anterior lobe extracts on dogs confirm the recent work on rats and mice (Evans; Smith) in establishing the fact that there are two distinct hormones.

1. *The growth principle.* Intraperitoneal injections in dogs cause in time a pathological overgrowth with splanchnomegaly, hyperplasia of thyroid and adrenal cortex in association with the following symptoms: polyphagia, polydipsia, polyuria, sialorrhea, lactation, asthenia and physical inactivity. In the females the genitalia become enlarged in the absence of oestrus; in males, testicular atrophy occurs and libido is diminished.

Chemically: no elevation of the basal metabolic rate has been demonstrated; blood cholesterol tends to be elevated; no observable change occurs in serum protein, in calcium, phosphorus or sugar. It has been shown, however (with O. Watkins of the Department of Biological Chemistry), that the non-protein nitrogen in the fasting blood falls approximately 25 per cent following injection of the growth principle.

2. *The sex principle.* Boiled dilute acetic acid extracts of very fresh bovine glands (anterior lobe), made according to the method described by Spaul (1924) for producing premature metamorphosis in salamanders, have brought about premature oestrus in twenty-six day old female rats. The ovaries enlarge though to a less extent than the enlargement produced by Smith's method of introducing living anterior lobe transplants. Not all extracts produced by this method have proved to be active but the results make it evident that the sex principle may sometimes be present in acid extracts which invariably destroy the growth principle.

DAUTREBANDE, L. et E. DELCOURT (BRUXELLES). **Sur un nouveau masque destiné à l'étude des échanges respiratoires en circuit ouvert.**

La détermination du métabolisme de base par la calorimétrie indirecte, pour être réalisée avec toute la précision voulue comporte un ensemble de nécessités techniques dont quelques-unes ont été étudiées par l'un de nous depuis plusieurs années.

Trois points principaux sont à considérer: 1°) l'espace nuisible 2°) la résistance et 3°) le confort.

Nous présentons aujourd'hui un masque fabriqué sur le modèle du masque à oxygénothérapie de Haldane. Il est muni de chaque côté de deux valves inspiratoires du modèle Rosling de petite taille et d'une valve expiratoire du modèle Rosling de grande taille.

1° *L'espace nuisible.* Ce qui compte dans un masque du point de vue physiologique ce n'est pas son espace nuisible physique ou son volume intérieur mais bien l'espace nuisible physiologique c'est à dire la quantité d'air expiré laissée dans le masque et reprise à l'inspiration suivante. Plus cette quantité d'air est considérable, plus augmente l'amplitude de la respiration. En raison de la courte distance qui sépare les narines de la bouche des quatre orifices d'inspiration, l'espace nuisible de ce nouveau masque est réduit à un minimum et si l'on suit un tracé kymographique de la respiration, on ne trouve pas de modifications après l'application de ce masque.

2° *Résistance.* Une résistance faible opposée à la respiration provoque, comme l'un de nous l'a montré, une augmentation du métabolisme de base.

Le fait d'avoir quatre portes d'entrée pour l'inspiration et une valve expiratoire très large rend la résistance de ce nouveau masque pratiquement nulle.

3° *Le confort.* En raison de l'impression d'air frais et de l'abolition de toute résistance le nouveau masque offre dans la majorité des cas une impression de confort très grand.

On peut mettre en évidence l'influence du manque de confort d'une manière simple. Il suffit de serrer exagérément les bandes occipitales qui assurent le maintien du masque pour voir le métabolisme s'élever. Si l'on fait deux déterminations de métabolisme l'une avec un masque DD₁ serré normalement et la seconde avec un masque DD₂ exagérément serré, on peut perdre dans ces conditions le bénéfice dû à la réduction de l'espace nuisible et de la résistance.

Application aux échanges respiratoires. Nous avons étudié le métabolisme de base de trente neuf sujets et quarante sept déterminations de métabolisme furent faites avec ce masque immédiatement avant ou

immédiatement après une autre détermination avec un masque ne présentant latéralement qu'une valve inspiratoire.

Ce masque à valve inspiratoire unique, utilisé dans plusieurs laboratoires depuis de nombreuses années, a toujours donné des résultats entièrement superposables aux chiffres étalons fournis par Aub et Du Bois pour sexe et âge donnés.

Nous avons pu constater que dans la plupart des cas les effets de la diminution de l'espace nuisible et de la résistance se traduisent par un abaissement des échanges nutritifs (le plus souvent avec diminution de la ventilation). Le métabolisme basal s'abaisse dans 85.5% des cas. La moyenne générale de l'abaissement du métabolisme basal tant sur les sujets normaux que chez les hypo et les hyperthyroïdiens soumis à l'expérience est d'environ 15%.

Dans 3% des cas le métabolisme basal est le même avec les deux masques.

Enfin dans 11.5% des cas nous avons obtenu avec le nouveau masque des métabolismes plus élevés, mais cette élévation était minime (3% en moyenne) et ne dépassait que de peu la sensibilité de la méthode.

Il est bien entendu que nous avons toujours rigoureusement contrôlé l'étanchéité de chaque masque.

DE CARO, LUIGI (NAPLES). *Peso Molecolare della Mioproteina.*

La tensione superficiale statica di soluzioni di mioproteina, (a lungo dializzata e diluita con acqua bidistillata in presenza di piccole quantità di NaOH) in funzione della diluizione, presenta tre minimi caratteristici alle seguenti concentrazioni: 1/37000; 1/55000; 1/80000; ciascuno dei quali minimi corrisponde a uno dei tre possibili orientamenti della molecola, considerata della forma di un parallelepipedo. L'esistenza di questi minimi permette di calcolare, secondo il metodo di Le Compte Du Noüy, le tre dimensioni fondamentali del parallelepipedo, e quindi il volume della molecola. Moltiplicando il volume per la densità si ha la massa, e moltiplicando questa per il numero di Avogadro, il peso molecolare, che risulta uguale a 2900000. Servendosi dei dati di analisi elementare della mioproteina di O. Fürth, e tenendo presente che H. Weber ha calcolato per la mioproteina un peso equivalente di 950, si può stabilire la composizione della molecola di mioproteinato sodico in corrispondenza di $\text{pH} = 9.0$, dalla quale risulta che un anione proteico può trasportare circa 3050 cariche elettriche.

Se si calcola la quantità in grammi di mioproteina, necessaria per rivestire di uno strato monomolecolare la superficie totale delle miofibrille esistenti in 1 cc. di muscolo (20000 cmq, secondo Bernstein), si trova che tale quantità corrisponde a poco meno della metà della quantità di mioproteina esistente in un grammo di muscolo, nel caso si consideri l'orientamento della molecola di mioproteina corrispondente al minimo di concentrazione di 1/37000, cioè con l'asse maggiore della molecola perpendicolare all'asse maggiore della miofibrille.

Nella molecola di mioproteina sono presenti gruppi polari e apolari, questi ultimi in prevalenza. Poiché le miofibrille sono ricche di lipidi, è verso di esse che saranno orientati i gruppi apolari, mentre i gruppi polari saranno orientati verso la fase acquosa sarcoplasmica.

Quando, in seguito a formazione di acido lattico, si ha la deionizzazione parziale o totale della mioproteina, le molecole perdono gran parte della

loro solubilità nella fase acquosa, e tendono ad aggregarsi. Ma poiché esse restano ancora, con l'altra estremità (apolare) ancorate alla fase lipoidea, la tendenza all'aggregazione dovrà sollecitare la deformazione della fase lipoidea nel senso di un accorciamento delle miofibrille.

DEFRISE, A. (MILANO). Ricerche di citologia quantitativa.

Non essendo possibile calcolare anche approssimativamente lo spessore di elementi cellulari fortemente appiattiti, quali quelli coltivati "in vitro," l'A. ha dovuto rinunciare allo studio di un rapporto tra volumi o tra volumi ed aree, del tipo di quello proposto e studiato da Cowdry ed Allievi in cellule di organi parenchimatosi.

Le variazioni degli indici $\frac{c.}{ct.}$ e $\frac{c.p.}{ct.}$ di elementi coltivati "in vitro" in rapporto alla diversa composizione del substrato nutritizio.

L'A. chiama $\frac{c.}{ct.}$ il rapporto tra l'area di un piano ideale che tagli la cellula nel senso della maggior larghezza e la somma delle aree di piani ideali condotti per gli spessori massimi delle masse del condriosoma; e $\frac{c.p.}{ct.}$ il rapporto tra la stessa area del citoplasma ed i perimetri delle aree

del condrioma. $\frac{c.}{ct.}$ e $\frac{c.p.}{ct.}$ vogliono convenzionalmente e rispettivamente esprimere il rapporto della massa e dell'estensione della superficie di reazione del condrioma rispetto al citoplasma.

I dati su cui furono condotti i calcoli, furono ricavati da disegni, eseguiti alla camera lucida, di cellule vitalmente trattate con verde Janus B, e colorate col metodo Altmann-Kull.

Le ricerche furono condotte su fibroцитi, e mioblasti coltivati a 38° in plasma, plasma-succo embrionale, in succo embrionale. Si calcolarono le variazioni dei rapporti $\frac{c.}{ct.}$ e $\frac{c.p.}{ct.}$ non solo nei confronti della diversa composizione di substrato, ma anche delle ore di coltura.

Dette variazioni sempre vennero raffrontate agli indici di crescita delle colture.

Scopo della ricerca fu quella di studiare il modo di comportarsi del condrioma—dal punto di vista quantitativo—di elementi di natura diversa a diverso metabolismo posti in simili o diverse condizioni ambientali, riferentesi, soprattutto, all'apporto di materiale nutritizio.

I dati ottenuti, che debbono essere intesi in senso relativo, permettono sintetiche valutazioni quantitative delle masse condriosomiche e possono riuscire utili per meglio intendere le modificazioni metaboliche degli elementi in esame.

I grafici, le considerazioni, le conclusioni, l'A. si riserva di comunicare al Congresso.

DEMOOR, JEAN et PIERRE RYLANT (BRUXELLES). Les réglages humoraux du coeur étudiés par la chronaxie.

L'Oreillette droite, dans du Locke, bat rythmiquement, réagit aux substances vagues et sympathiques et est normalement sensible.

L'Oreille gauche ne manifeste aucune de ces propriétés, et y produit des secousses apériodiques. Elle s'y sensibilise rapidement après l'addition au liquide d'un extrait de tissu nodal (*Substances actives*), et dès lors aussi, bat rythmiquement.

Pour définir la chronaxie du tissu cardiaque nous lui imposons un rythme accéléré et y éveillons des extrasystoles intercalées, inotropiquement faibles suivies d'un repos prolongé que termine une contraction exagérée témoignant de l'efficacité de l'excitant. La valeur de l'excitation minimale opérante définit la chronaxie.

Grâce à cette méthode, nous avons obtenu pour les oreillettes travaillant dans du Locke, les valeurs suivantes.

I.—Oreillettes, droite ou gauche, soit inertes soit rythmées par les substances actives (Rythme imposé = 240 à la minute): Chronaxie = 2σ .

II.—Oreillettes, droite ou gauche rythmée par les substances actives, (Rythme imposé = 240) avec adrénaline: Chronaxie 2, 5σ avec acétylcholine: Chronaxie 1σ .

III.—Oreille droite ou gauche rythmée par les substances actives, (rythme imposé: 240) avec substances vagues: Chronaxie 1,0; avec substances sympathiques: Chronaxie: $2,5\sigma$.

Les substances actives, qui rythment l'oreille gauche, sans la fatiguer et en lui donnant toutes les caractéristiques d'irritabilité, ne modifient pas la Chronaxie.

Les agents humoraux surgissant dans le coeur lors du travail du vague ou du sympathique, ou leurs mimétiques, acétylcholine ou adrénaline, dont l'activité fatigue et est troublée par l'atropine ou l'ergotamine, diminuent ou augmentent la Chronaxie.

Deux réglages humoraux opèrent dans le coeur. Les substances actives déterminent l'automatisme rythmé en agissant comme conditions de vie. Les substances mimétiques du travail des nerfs extrinsèques, véritables facteurs d'irritabilité, modifient l'automatisme sans altérer ses caractères fondamentaux.

DE WAELE, H., J. VANDEVELDE et L. BRAYE (GAND). **L'origine et le trajet des vasodilatateurs des racines postérieures.**

En 1877 Stricker signale une action vasodilatatrice produite par l'excitation des racines postérieures. Une action efférente des racines postérieures étant en contradiction avec la loi de Magendie, il y a discussion. Des auteurs ont cherché des fibres efférentes par diverses méthodes, mais en 1901 Bayliss signale que ces fibres ont exactement la même distribution que les nerfs sensibles et ont leur cellule dans le ganglion vertébral, donc il n'est pas démontré qu'il y ait des fibres spéciales pour cette action vasodilatatrice.

D'autres auteurs ont cherché une relation avec le sympathique d'après Werzilloff, Tofanow et Tschalussow la vasodilatation est encore possible après section du sympathique abdominal, tandis que d'après Dastre et Morat une excitation du sympathique abdominal immédiatement sous le diaphragme donne de la vasodilatation. Donc ici encore désaccord.

Entretemps Laffont cherchant les voies d'un réflexe de Loven (vasodilatation dans une partie endolorie et vasoconstriction générale) montre que les vasodilatateurs de la patte sont en rapport avec les ggl. symp. abdom. supérieurs, tandis que l'on sait par les travaux de Bayliss et Bad-

ford et de Langley, que la vaso constriction est en rapport avec les ggl. symp. abdom. inférieurs.

D'après nos expériences la vasodilatation par l'excitation des racines postérieure l'se produit si l'anesthésie n'atteint pas la disparition du reflexe cornén, 2° elle est bilatérale et 3°. il faut que les racines postérieures voisines soient intactes. D'où il ressort que la voie est la suivante: conduction antidromique vers la périphérie, perception douloureuse qui se réfléchit (par anastomose ou par production de substances algogènes diffusibles) et remonte par les racines postérieures voisines aux centres vasomotéurs. L'excitation redescend par la moelle, les rameaux communicants blancs, gangl. lymph. abd. supér, ram. comm. gris et nerf mixte. En effet l'extirpation des gangl. Symp. abd. infér n'empêche que la vaso constriction, tandis que l'extirpation des ggl. symp. abd. supér. supprime la vasodilatation.

Ainsi tandis qu'une excitation des racines antérieures donne une action centrifuge directe, une excitation des racines postérieures fait par reflexion d'une sensation douloureuse modérée, de la vaso dilatation locale, et de la vasoconstriction générale. Une douleur forte fait prédominer cette dernière.

La vasodilatation par excitation des racines postérieures serait donc un cas particulier d'un réflexe de Loven.

DILL, D. B. and J. H. TALBOTT (BOSTON). **Oxygen Dissociation Curves and Sodium and Potassium Distribution.**

The concentrations of sodium and of potassium have been determined by A. O. A. C. methods¹ in serum and cells of blood of 5 species of mammals. The same specimens of blood were equilibrated with suitable mixtures of carbon dioxide and oxygen and data obtained for construction of oxygen and of carbonic acid dissociation curves.

From carbonic acid dissociation curves, calculated values for pH_c (assuming $pK'_c = 5.93$) were plotted against $\log pCO_2$. The pH_c value corresponding to each point on the oxygen dissociation curves was obtained by interpolation. In most cases several oxygen dissociation curves were derived for each specimen of blood. These curves were transformed to $pH_c = 7.10$ making use of the fact that a curve may be accurately shifted from one hydrogen ion concentration to another by multiplying the oxygen pressure values by a factor which is a linear function of pH_c .

The following summary compares sodium and potassium concentrations² with position³ of the oxygen dissociation curve corresponding to $pH_c = 7.10$.

¹ Methods of Analysis of the Association of Official Agricultural Chemists—Washington, 1925.

² Concentrations are in terms of mM per kgm. water.

³ The position is defined as the oxygen pressure in mm. of Hg when $pH_c = 7.10$, temp. = 37.5°C. and $HbO_2 = 50$ per cent.

	POSITION OF OXYGEN CURVE	(Na) _s	(K) _s	(Na) _c	(K) _c	$\frac{(Na)_c}{(K)_c}$	$\frac{(Na)_s + (K)_s}{(Na)_c + (K)_c}$
	mm. Hg.						
Sheep 1.....	42.8	161.4	7.9				
Sheep 3.....	33.1	159.0	6.4	141.1	18.3	7.7	1.03
Sheep 4.....	42.1	159.0	10.3	135.0	23.0	5.9	1.07
Sheep 5.....	38.0	160.5	9.9	146.0	16.0	9.1	1.05
Sheep, average.....	39.0	159.9	8.6	140.7	19.1	7.6	1.05
Pig, average.....	33.7	147.4	4.9	26.0	158.7	0.17	0.83
Ox, average.....	29.8	157.2	5.5	97.0	42.1	1.9	1.08
Man, average.....	27.0	147.8	3.7	22.3	126.2	0.18	1.02
Horse, average.....	25.6	146.8	3.6	29.8	138.9	0.21	0.89

A large variation in position of the oxygen curve may occur without obviously related changes in sodium and potassium concentrations. Differences in sodium and potassium concentrations may be extreme without great change in oxygen dissociation curve. Difference in the nature of hemoglobin in different species and even within the same species appears to be the most probable explanation of the differences found.

DINGEMANSE, ELISABETH (AMSTERDAM). **Über Adsorption an Kohle im besonderen an Medizinal-Supra-Norit.**

Die Erfahrungen eigener früherer Untersuchungen, wobei sich unter verschiedenen Kohlsorten die Medizinal-Supra-Norit als die best adsorbierende Kohle zeigte, wurden durch Versuche über das Verhalten in vivo ergänzt und zwar in zweierlei Weise.

a. Es wurde an Kohle die daran maximal festzulegende Menge Methylenblau in vitro adsorbiert und die auf diese Weise belastete Kohle sowohl Menschen wie Hunden oral gegeben. Hierbei zeigte sich, dass sehr starke individuelle Unterschiede vorhanden sind hinsichtlich des Endes der Zeit, während welcher überhaupt Methylenblau sich ablöst, also ausgeschieden wird. Das Wichtigste ist aber, dass bei bestimmter Sorte Medizinal-Supra-Norit, obwohl dann per Gramm Kohle-Methylenblau-Gemisch absolut am meisten Methylenblau enthalten ist, sich überhaupt kein Methylenblau im Harn nachweisen liess, also nichts losgelassen wird. Die Merck'sche Kohle kam in einzelnen Versuchen diesem Ideale nahe.

b. Es wurde erst Methylenblau per os gegeben und 10 Minuten später Kohle. Hierbei zeigte sich, dass im günstigsten Falle 60 Procent der Menge, die in vitro überhaupt an der Kohle hätte adsorbiert werden können, festgelegt, also an der Ausscheidung verhindert wird.

Mit Strychnin an Mäusen zeigten sich grundsätzlich gleiche Ergebnisse.

Es stellte sich ferner heraus, dass nur mit Supra-Norit-Kohle, und zwar bestimmten Mustern hiervon, Insulin (Organon) sich soweit reinigen liess, dass die internationale Einheit, soweit uns bekannt, bisher in kleinster Menge, nämlich in 6 γ enthalten war.

DOISY, EDWARD A., C. D. VILER and S. THAYER (ST. LOUIS). **Folliculin from Urine of Pregnant Women.**

A study of the extraction of folliculin from urine has shown that chloroform and olive oil are the best solvents of those tested. Using chloroform

and a continuous liquid extraction apparatus, large quantities of the crude extract have been prepared. The apparatus used permits the extraction of about 30 liters of urine per 24 hours with a recovery of over 75 per cent of the hormone. The crude extract is refined according to the principles outlined below.

The extraction with olive oil has proved to be quite satisfactory, about 50 per cent of the folliculin being removed by stirring the urine for $\frac{1}{2}$ hour with an amount of olive oil equal to $\frac{1}{20}$ of the volume of urine. The hormone is then transferred to ethyl alcohol, the concentration of alcohol reduced to 70 per cent with water, and the alcoholic solution extracted with petroleum ether. The alcoholic solution is distilled, the residue dissolved in butyl alcohol and this alcoholic solution extracted with dilute sodium hydroxide. The butyl alcohol is distilled, the residue leached with ethyl ether, the ether distilled and the residue dissolved in butyl alcohol. Petroleum ether is added and the precipitate discarded. The hormone is then extracted from the butyl alcohol-petroleum ether solution with dilute acids or alkalies. Separation of the hormone from the aqueous solution and a repetition of the aqueous extraction has given a product of which 1 rat unit weighs less than 0.001 mgm.

An attempt to apply the procedure described for the preparation of aqueous solutions from liquor folliculi to urines, resulted in failure. This failure of the liquor folliculi method might have been due to either *a*, a difference in the contaminating substances, or *b*, a chemical difference between the physiologically active substances of liquor folliculi and urine. In line with the latter possibility is the paradoxical situation of the large amount of folliculin in the blood and urine during pregnancy, yet the reports of abortion produced by injections of the oestrous hormone. Working with the highly purified preparations (1000 R. U. per mgm.), we can say that the solubilities give no reason for doubting the identity of the two products. In addition, a certain set of reactions of the hormone from the two sources with benzoyl chloride and α -naphthyl isocyanate yields the same results.

A crystalline product which has been recrystallized several times has been isolated from the urine. The assays show that the crystals are physiologically more active than any preparations obtained thus far, the activity being more than 2000 rat units per milligram.

Since our evidence, both chemical and physiological, points to the identity of the active material of the liquor folliculi and urine, and the simple procedure of preparation described yields a very pure product from a readily available, cheap source, clinical and experimental work with the oestrous hormone will be greatly expedited.

DOOLEY, M. S. and C. J. WELLS (SYRACUSE). Circulatory, Respiratory and Other Reflexes Induced by Inhalation of Irritant Anesthetics.

Comparison of the volatile anesthetics shows that only the irritant types induce the following marked reflex changes on inhalation: inhibition of respiration and heart; vasoconstriction; salivation even when kept from contact with the mucous membranes of nose, mouth, pharynx and larynx; dilatation of pupil even when applied only to the upper part of the respiratory tract (from lower limit of larynx upward). The non-irritant types locally applied induce none of these effects.

An important phase of the above mentioned vasoconstriction is that of the spasm of the renal vessels, sometimes of long duration. This leads to anuria which may be permanent even though normal kidney volume may be re-established. A more crucial test of the reflex nature of the kidney vessel spasm is that amyl nitrite, a drug known to dilate these vessels on direct contact, constricts them as readily as does ether when applied to the upper part of the respiratory tract. It is suggested that this reflex effect on the kidney may account for the so-called "ether anuria" encountered clinically.

The only unusual technical procedure used was that of double cannulation of the trachea, the upper of the two directed upward to facilitate the application of gases to the isolated upper part of the tract.

DOWNING, A. C. and A. V. HILL (LONDON). **Heat-Production of Nerve. (Demonstration)**

DOWNING, A. C. and J. L. PARKINSON (LONDON). **Myothermic and Other Apparatus. (Demonstration)**

DRAGSTEDT, LESTER R. and JAMES C. ELLIS (CHICAGO). **The Fatal Effect of the Total Loss of Gastric Juice.**

The stomach was isolated by section at the cardia and pylorus. The duodenum was anastomosed to the lower end of the esophagus. The cardiac end of the isolated stomach was closed and the pyloric end brought to the surface as a fistula. Care was taken not to interfere with the vagus nerves or blood vessels supplying the isolated stomach. Six dogs were prepared in this manner and observations made on the amount and quality of gastric secretion and accompanying changes in the blood chemistry. The following points have been established:

1. The total loss of the gastric secretion from the body causes death in the dog in five to eight days with symptoms of weakness, anorexia, loss of weight, oliguria, and profound depression.

2. Accompanying these symptoms and proportionate to their severity there occurs a decrease in the concentration of blood chloride (340 to 108 mgm.), an increase in the CO_2 capacity (45 to 140 cc.), an increase in the pH (7.30 to 7.75), and a terminal increase in non-protein nitrogen (27 to 180 mgm.) and urea N (12 to 154 mgm.).

3. The symptoms may be relieved, the blood chemistry returned toward the normal, and life prolonged by the intravenous injection of 2000 to 3000 cc. of Ringer's solution per 24 hours. In no case, however, has life been prolonged over 76 days.

4. The isolated stomach, with intact blood and vagal supply, will secrete in 24 hours from 1000 to 2600 cc. of gastric juice with a chloride concentration of 0.50 per cent to 0.55 per cent, free HCl 0.45 per cent, and total HCl 0.50 per cent. There is thus excreted by the gastric mucosa in 24 hours from two to three times the calculated amount of chloride ion in the circulating blood.

5. The gastric glands can continue to secrete gastric juice of high free and total acidity (0.31 per cent and 0.36 per cent respectively), even when the blood chloride has been reduced to less than a third of its normal concentration (108 mgm. of Cl per 100 cc.) and an extreme alkalosis exists (plasma CO_2 104 and pH 7.70). Under these conditions, however, the volume of secretion is lessened (300 to 500 cc. per 24 hours). This is a

continuous secretion, however, since the animal is depressed and refuses food. The ordinary stimuli for secretion are thus absent.

6. When, as a result of alkalosis, hypo-chloremia, dehydration and absence of food taking, the volume of juice is depressed, the intravenous injection of Ringer's solution causes a pronounced increase in secretion (from 300 cc. per 24 hours to 1500 cc.), and this without the stimulus of food.

7. The body temperature remains normal throughout the periods of dehydration.

8. There has been no evidence of tetany at any time, the deviation from the normal being in the direction of depression rather than excitation.

DRAGSTEDT, LESTER R. and JAMES C. ELLIS (CHICAGO). Specimen Showing the Isolated Entire Stomach of the Dog with Intact Blood and Vagal Supply. (Demonstration)

DRASTICH, L. (BRNO). Sur la concentration en hémoglobine dans les globules rouges de différentes espèces animales.

Depuis environ deux ans, je fais des recherches sur la concentration en hémoglobine dans les globules rouges de différentes espèces animales. Ma méthode est très simple.¹ On détermine à l'aide de l'hématocrite le pourcentage des globules rouges du sang /ev/. J'ai construit dans ce but un hématocrite spécial, qu'on peut utiliser avec chaque centrifugeuse. En même temps, on évalue la quantité, en grammes, d'hémoglobine /h/, contenue dans 100 cc. de sang. J'ai obtenu de bons résultats par la micro-méthode de Bürker. Les colorimètres du modèle de Gowers ou Sahli se sont montrés moins précis. La concentration d'hémoglobine, K est calculée ensuite par cette formule:

$$K = \frac{h}{ev} \cdot 100$$

Chez un Homme jeune, en bonne santé la concentration d'hémoglobine dans les globules rouges ne subit que de très faibles variations. En examinant 11 sujets, j'ai obtenu les chiffres suivants: 33,7; 34,5; 34,3; 34,1; 34,1; 34,5; 34,1; 33,—; 33,—; 34,65, 33,72. La moyenne est de 34 gr d'hémoglobine pour 100 cc. des globules rouges. Chez les hommes atteints d'anémie pernicieuse, la concentration d'hémoglobine est à la limite supérieure de la concentration normale, comme le montrent les chiffres suivants: 36,—; 34,9; 35,1; 35,8; 35,3; 34,8. Ce qui élève la valeur globulaire, en cas d'anémie pernicieuse, c'est l'augmentation du volume des hématies, et non pas l'augmentation considérable de la concentration en hémoglobine. Dans des cas d'autres anémies, j'ai vu baisser cette concentration jusqu'à: 28,—; 26,4; 25,7; même à 23,3.²

Dans la première série de mes expériences, j'ai admis que ce taux subissait des variations beaucoup plus grandes. C'est pourquoi je supposais que la concentration en hémoglobine était la même pour tous les espèces, mais pouvait subir des variations plus ou moins importantes. Mais des recherches précises, sur un plus grand matériel, ont montré que, chez quelques espèces animales, la concentration en hémoglobine est moins

¹ Pflüger's Arch., 1928, ccix, 227. Compt. rend. Soc. Biol., 1927, xcvi, 266.

² Compt. rend. Soc. Biol., 1928, xcix, 991.

forte. Jusqu'ici j'ai étudié 9 lapins sains. Les chiffres obtenus sont les suivants:

LAPIN N°.	HÉMOGLOBINE EN GR. DANS 100 CC. DE SANG	VOLUME DES HÉMATIES P. 100	CONCENTRATION D'HÉMOGL. GR. P. 100 CC. DES HÉMATIE
1	10,4 10,2	34,- 34,-	30,7 30,- après 1 heure
2	10,8 11,-	37,- 37,5	29,2 29,4 après 1 heure
3	9,85 6,7	33,- 22,25	29,8 30,1 après anémie provoquée par le B. perfringens
4	9,3	32,-	29,-
5	9,7 10,-	35,5 36,-	27,3 27,8 après 1 heure
6	11,9 11,9	38,5 37,5	31,- 31,8 après 1 heure
7	11,5	36,5	31,5
8	11,3	40,-	28,2
9	11,7	38,-	30,8

La moyenne est de 30; le taux le plus bas de 27,3, le plus élevé de 31,8. Ces chiffres sont nettement inférieurs à ceux qu'on trouve chez l'homme.

Il va sans dire que la concentration en hémoglobine chez les Vertébrés à hématies nucléées est plus basse à cause du noyau de ces hématies. C'est à dire, chez les oiseaux: 29,5, Batraciens; 24,8, Poissons: 26,—.

Résumé: Ces expériences montrent que la concentration en hémoglobine dans les globules rouges du lapin est plus basse que chez l'homme. De nouvelles expériences devraient être entreprises pour préciser si ce fait est dû à la vie de cet animal à l'abri des rayons directs du soleil, ou à toute autre influence.

DRESBACH, M. (ALBANY). The Emetic Action of Digitalis Bodies after Attempted Denervation of the Abdominal Viscera.

The author has reported experiments¹ dealing with the emetic action of digitalis bodies in cats with denervated hearts and it was brought out that the denervation does not prevent emesis. In the present work the attempt has been made to denervate the abdominal organs and peritoneum by dividing the vagi and splanchnic nerves below the diaphragm, and by severing the spinal cord above the origin of the splanchnics and the vagi below the diaphragm. Before and after the operations the cats were tested with certain emetics of the class mentioned. In a series of twenty-one animals five died before the emetics could be given after the operations and the remainder lived long enough to react to one or more of the drugs,

¹ Preliminary report, 12th International Physiological Congress, Stockholm, 1926; also, with K. C. Waddell, Journ. Pharm. Exper. Therap., 1926, xxvii, 9; Journ. Lab. and Clin. Med., 1929, xiv, 625.

which included k-strophanthidin, ouabain, digitoxin, tincture of digitalis and copper sulphate. The latter emetic was given by stomach tube and the others intraperitoneally, intramuscularly or intravenously. The k-strophanthidin was sometimes given to one and the same cat by all of the latter three methods.

In thirteen of the cats vomiting was produced by one, several or all of the above substances, and copper sulphate induced emesis in six cats. It made no difference how the digitalis bodies were given, whether by one route or the other. Post-mortem examination of the animals showed that we could not be certain in any case that denervation had been complete but we regard it as significant that in only three of sixteen animals did we fail to induce vomiting. In view of the fact that emesis was not prevented by fairly extensive injury to certain afferent tracts and complete blocking of the remaining ones, and since the emesis occurred after intramuscular and intravenous injections, it seems very doubtful whether the vomiting was due to stimulation of afferent nerve endings in the abdomen.

The fact that copper sulphate induced vomiting in some cases suggests that afferent paths from the stomach and intestines were intact, but we have shown (*loc. cit.*) that these paths are not necessary for digitalis emesis. Therefore, the exact seat, or seats, of the emetic action of digitalis bodies is still undecided.

DRINKER, C. K., A. B. VAN WOERT and R. M. THOMSON (BOSTON).
An Installation for Making Observations on Men Living under High and Low Atmospheric Pressures. (Demonstration)

DRINKER, C. K. and STEPHEN WENT (BOSTON). **A Method for Measuring Pulmonary Arterial Pressure in the Guinea Pig. (Demonstration)**

DU BOIS, E. F., W. S. MCCLELLAN, H. J. SPENCER and E. A. FALK (NEW YORK). **Metabolic Observations on Two Men who Received Exclusive Meat Diets.**

Two arctic explorers have been observed for a period of one year during which they ate nothing but meat. Studies were made of these men before, during, and after the time when they received the meat diets. The diet included beef muscle, tongue, liver, kidney, brain, fat and bone marrow; also veal, lamb, pork, and chicken. The fluids taken were meat broths, black tea, and water. The daily consumption of protein varied between 100 and 135 grams, of fat 175 and 250 grams, and of carbohydrate (contained in meat) 5 and 10 grams. The diet was distinctly acid in nature and was deficient in calcium.

The men lost 2 to 3 kgm. in weight during the first month after which their weight remained constant. No elevation in blood pressure occurred. The kidneys showed no evidence of damage. There was an increase of fat and cholesterol in the blood during the early periods of the observations but no change in the nitrogenous elements was noted. In the urine the acetone bodies were found continuously in small amounts, 0.5 to 5.0 grams per day and the acidity was 2 to 3 times greater than when they were receiving mixed diets.

The basal metabolism remained at the same level between -10 and -20 per cent of normal. The effects of protein, of fat and of carbohydrate meals were studied. The specific dynamic action of protein was slightly

greater at the end of the meat diet. The carbohydrate tolerance test with 100 grams of glucose at the end of the meat diet showed a tendency toward a sustained elevation in the level of the blood sugar. Negative calcium and phosphorus balances occurred even with the high phosphorus content of the food. The blood calcium remained constant. There were no signs of avitaminosis or any other injurious results of this diet. These men remained physically and mentally normal.

DUCUING, J. et L. C. SOULA (TOULOUSE). **Périphlébites expérimentales.**

Des périphlébites réalisées expérimentalement ont permis de montrer par l'exploration radioscopique et radiographique au lipiodol l'importance du spasme veineux.

DUCUING, ROUZAUD, SOULA et BOUISSET (TOULOUSE). **Stase hépatique et glycémie. (Démonstration)**

L'obstruction des veines sushépatiques détermine une hyperglycémie. Cette hyperglycémie relève de la carence insuliniennne.

DUSSER DE BARENNE, J. G. (UTRECHT). **The Syndrome of the Local Strychninisation of the Dorsal Sensory Mechanisms of the Spinal Cord.**

Notwithstanding many experimental trials the author had formerly (1911-1913) not succeeded in establishing whether in the syndrome of the local strychninisation of the dorsal spinal mechanisms, besides the sensory disturbances in the skin, disturbances of the sensitivity of the deeper structures are also present or not. As they could be shown to occur in the strychnine-syndrome of the sensory cerebral cortex, this point was once more investigated.

In the normal animal the disturbances of the cutaneous sensibility after local spinal strychninisation are so intense (both the spontaneous paraesthesia as well as the reactive disturbances), that probably they thereby overwhelm the other disturbances. In any case the earlier experiments in animals with intact central nervous system were not conclusive upon this point.

In the *decerebrate* cat it could be shown very clearly that on local strychninisation of the dorsal mechanisms of the lumbar spinal cord the mechanical stimulation of certain muscles, tendons and probably also of the periost, gives rise to distinct reactions of the preparation, of the same kind as occur on stimulation of the skin in the strychnine-segment-zone. Special care was taken of course not to stimulate the skin, when applying the stimulus to the deeper structures. Mostly this was done by destroying cutaneous sensibility by section of the nerves to the skin. From these results it follows that in the syndrome of the strychninisation of the spinal sensory mechanisms disturbances of the "deep" sensibility also have their place.

This syndrome, therefore, can now be given as follows:

1. Paroxysmal, paraesthetic disturbances, occurring without any external stimulus, even after degeneration of the posterior roots.
2. Hyperaesthesia and hyperalgesia of the skin (in the corresponding strychnine-segment-zone).
3. Hypersensitivity of the deeper structures (muscles, tendons and probably of the periost, according to the strychninised segment).

4. a. Hypereflexia.

b. Muscle twitches or contractions, occurring without any appreciable external stimulus; these contractions are still for the greater part reflex, as they are much depressed by section of the posterior roots.

EBBECKE, ULRICH (BONN). **Über die Änderung der elektrotonischen Ströme und der Nervenregbarkeit nach längerdauernder Durchströmung.**

Der anelektrische Strom ist, wie bekannt, stärker und ausgebreiteter als der katelektrotonische; jener nimmt mit der Dauer der Durchströmung zu, dieser ab. Deutung im Sinne der Membrantheorie als polar entgegengesetzte Verdichtung und Auflockerung und Polarisierbarkeitsänderung. Vgl. *Woronzow* und *Mackuth*. Hierzu treten ergänzend: 1) die gleichzeitig eintretende und parallel gehende Zunahme (Abnahme) des lokalen anodischen (kathodischen) Widerstandes und des anelektrotonischen (katelektrotonischen) Stroms; 2) das analog Verhalten elektrotonischer Hautströme; 3) die, eine Durchströmung längere Zeit überdauernde Nachwirkung, Herabsetzung der an- und katelektrotonischen Ströme in der Nachbarschaft der früheren Kathode, Steigerung in Nachbarschaft der Anode. Zu 1) wird mittels 4 Elektroden kontinuierlich minuten- oder stundenlang die Stärke des polarisierenden und die Stärke und Spannung (Kompensationsmethode) des elektrotonischen Stroms registriert. 2) wird mit 4 auf die menschliche Haut gesetzten Flüssigkeits-elektroden gemessen. Zu 3) werden die durch gleiche Spannung erzeugten an- und katelektrotonischen Ströme vor und nach längerer anodischer oder kathodischer Durchströmung miteinander verglichen. Das Resultat zeigt die depressive Kathodenwirkung und die restituierende Anodenwirkung und gibt eine Erklärung dafür, dass nach längerdauernder Durchströmung der 3. Fall des Pflüger'schen Zuckungsgesetzes schon bei verhältnismässig schwachen Strömen erreicht wird und dass eine vorangegangene Durchströmung die Schwelle für die Anodenöffnungszuckung erheblich und für längere Zeit herabsetzt, welche Wirkung parallel mit der Änderung des elektrotonischen Stroms allmählich zurückgeht.

EBBECKE, ULRICH (BONN). **Demonstration elektrotonischer Hautströme am Menschen. (Demonstration)**

Mit vier auf die Haut des Unterarms applizierten Flüssigkeitselektroden, von denen die beiden mittleren untereinander verbunden sind, wird ein elektrotonischer Strom abgeleitet, wobei der anelektrotonische Strom zugleich mit dem Anwachsen des Anodenwiderstandes steigt, der katelektrotonische Strom unter kathodischer Widerstandsabnahme sinkt. In der intrapolaren Strecke wird der Spannungsabfall und der Indifferenzpunkt gezeigt, welcher letzterer sich, je stärker und anhaltender der Strom ist, umso mehr, nach der Seite der Kathode verschiebt. Analogie zu den elektrotonischen Nervenströmen.

ECKER, E. E. (CLEVELAND). **Demonstration of the Effect of Certain Toxic Substances in Bacterial Cultures on Intestinal Movement. A Cinematographic Study.**

EDERER, STEFAN (BUDAPEST). **The Specific Dynamic Action and the Vegetative Nervous System.**

EDWARDS, D. J. and McKEEN CATTELL (NEW YORK). **Effects of Pressure on the Tension Curve of Heart Muscle.**

The application of pressure to cardiac or skeletal muscle through a fluid medium in which the tissue is completely immersed greatly augments its functional activity, thus contrasting with the influence of pressure locally applied which causes a suspension of activity due to deformation and fluid displacement. In previous reports we have shown that a hydrostatic pressure of 882 pounds per square inch markedly stimulates the contractile force exerted by the heart, shortens the cycle time, and improves conductivity. In the case of striated muscle a pressure of 1000 pounds per square inch resulted in an average increase in the tension developed by a single twitch of 32 per cent, and produced a corresponding increase in the heat production. The heat-tension ratio remained constant throughout the range down to atmospheric pressure; whereas the total energy set free was directly proportional to the pressure employed.

Further experiments have been carried out using portions of the ventricle from the heart of the turtle and employing a tension lever for the recording. In twenty experiments in which this preparation was employed the average increase in tension resulting from the application of 1000 pounds per square inch was 35.8 per cent. Observations have been made also, on a preparation of the auricular muscle using higher pressures. In this series of experiments the entire auricle was employed and subjected to pressures between 1400 and 1600 pounds per square inch. The average augmentation of contraction by pressures in this range amounted to 124.5 per cent in twelve experiments.

While pressure increases markedly the amount of tension that the heart develops, the time required in getting up the greater contractile stress is increased very little over the normal duration of contraction. The phase of relaxation, on the other hand, is prolonged as shown by an average increase of 8.8 per cent in twenty experiments. This can be adequately explained by the greater mechanical changes required by the larger responses, and probably does not represent a specific influence of pressure.

In experiments in which the well-known action of a change in the temperature of the muscle has been used to alter the extent and duration of contraction it has been shown that pressure still produces the usual additive effect on the amount of tension the muscle is capable of developing. Lowering of the temperature from 5 to 10° has the effect on the muscle of increasing the power of developing tension, and raising the temperature about 5° has the reverse action. In eight experiments using cooled ventricles the average increase in the tension recorded amounts to 33.7 per cent. Pressures of 1000 pounds per square inch applied to these preparations gave an additional increase of 19 per cent, making a combined increase in tension of 52 per cent for the cooled hearts, in contrast to the normal augmenting action of pressure of about 32 per cent at room temperature.

The observation that the duration of the augmented contraction produced by pressure is not significantly increased, and that the usual stimulating effect of pressure can be superimposed upon the augmented action from cooling, support the view that the mechanism of the pressure effect is not simply that of changing the time scale of the process of contraction.

ELLINGER, PH. und A. HIRT (HEIDELBERG). **Mikroskopische Untersuchungen an lebenden Organen. (Demonstration)** Demonstriert von Ph. Ellinger.

Es wird eine Methode beschrieben, um lebende Organe von Amphibien.

Reptilien und Säugetieren mit stärksten mikroskopischen Vergrößerungen zu beobachten. Sie beruht darauf, dass den Tieren Fluorescein und Trypaflavin in das Unterhautzellgewebe oder unmittelbar in die Blutbahn injiziert wird. Die Beobachtung erfolgt durch Beleuchtung mit ultravioletttem Licht mittels Opak-Illuminator bei Verwendung von Wasserimmersionen. Serum und bestimmte Zellen bzw. Zellbestandteile nehmen den Farbstoff auf und geben durch das Fluoreszenzlicht eine so intensive Beleuchtung des Organs, dass es mit stärksten mikroskopischen Objektiven beobachtet werden kann. Neben der Beobachtung der Funktion einzelner Organe, (Niere, Leber, Lunge, Pankreas 1 Drüsen, Zentralnervensystem) in der Norm und unter dem Einfluss verschiedenster Eingriffe und Pharmaka, gelingt es auch den Ausscheidungsmechanismus für Fluorescein, Trypaflavin und andere Farbstoffe in der Niere und den Gallenwegen festzustellen. Weiterhin wurden Untersuchungen über die Strömungsverhältnisse in kleinen Gefässen angestellt.

EMBDEN, GUSTAV und MARGARETE LEHNARTZ (FRANKFURT A.M.).
Über den Abbau und Wiederaufbau einiger Tätigkeitssubstanzen bei der Arbeit isolierter Muskeln.

Es wird über das Verhalten verschiedener Tätigkeits-substanzen des Muskels bei der Kontraktion und der daran sich anschliessenden Erholung berichtet.

1. Namentlich wurde das Verhalten des Lactacidogens und der Pyrophosphorsäure bei der Muskelarbeit getrennt verfolgt. Hierbei ergab sich, dass der bei der Tätigkeit eintretende Abbau beider Substanzen unter geeigneten Bedingungen auch im isolierten Muskel von ihrem Wiederaufbau gefolgt ist.

2. Die zeitliche Aufeinanderfolge der Spaltung und der Resynthese beider Substanzen wird erörtert.

ENDRES, G. (WÜRZBURG). **Ungleiche Empfindlichkeit der Fasern afferenter Hautnerven gegen anästhesierende Stoffe.**

Es werden Hautnerven (N. cut. femor. antr., N. cut. antibrachii dors.) am Orte ihres Durchtritts durch die Faszie mit schwachen Lösungen von Tutokain (bzw. Kokain) + Adrenalin umspritzt. Es verschwinden der Reihe nach die Kalt-, Warm-, Schmerz- und Druckempfindung im Verteilungsgebiet dieser Nerven. Die Rückkehr der Empfindungen geschieht in der umgekehrten Reihenfolge. Die Vertäubung beginnt zuerst an der Injektionsstelle und schreitet dann in schuppenartig aneinander grenzenden Querzonen gegen das distale Ende des Versorgungsgebietes des Nerven fort. Bei dem Vertäubungsgang lassen sich drei Phasen unterscheiden: Die Vertäubungszeit (Zeit der schwindenden Empfindungen), die Zeit der vollständigen Lähmung und die Enttäubungszeit (Zeit der sich wieder einstellenden Empfindungen).

Die Versuche zwingen zur Annahme, dass die Nervenfasern im Stamm besonders angeordnet sind, dass weiterhin die Fasern der verschiedenen Sinnesqualitäten eine verschiedene starke Affinität zum Narkotikum haben, sich also unter sich durch eine verschiedene Struktur auszeichnen.

ERLANGER, JOSEPH and H. S. GASSER (ST. LOUIS). **The Action Potential in Fibers of Slow Conduction in Spinal Roots and Somatic Nerves.**

When use is made of greater amplification (100,000 instead of 8,000),

longer recording times, and stronger stimuli than heretofore employed by us, the cathode ray oscillograph discloses in conducted action potentials, in addition to the *alpha-beta-gamma* group of waves, now collectively named *A*, two discrete, often compound, elevations, one, *B*, travelling at rates ranging between 5 and 3 m.p.s. in the frog (room temperature) and 17 and 11 m.p.s. in the dog (body temperature), the other, *C*, between 0.7 and 0.3 in the frog and 1.5 to 0.8 m.p.s. in the dog, the range of rates of the component *A* fibers in these species being, roughly, 40 to 10 and 80 to 30 m.p.s. Induction shocks threshold for *A*, *B* and *C* may have amplitudes of 3, 7 + and 38 volts, shocks maximal for *B* and *C*, 38 and 80 volts. The relative and absolute amplitudes of *A*, *B* and *C* differ with the nerve and with the distance of conduction; typical values are, in the frog's sciatic at 91 mm. of conduction, 174, 10 and 4.5 mm., in the dog's saphenous at 70 mm., 154, 20 and 5 mm. The elevations are well developed in skin nerves. In the phrenic nerve *B* is absent or small; in other muscle nerves of the dog *B* is variable, while in those of the frog it is prominent.

The somatic action potential in the bullfrog derives its *A* components from the anterior and posterior roots (6th to 9th studied), its *B* components from the grey rami, and its *C* components from the grey rami, the posterior, and some of the anterior roots. In the cat, *A* components are supplied by the anterior and posterior roots (7th lumbar and 1st sacral studied), and *C* components by grey rami and posterior roots; the *B* elevation comes from the grey rami.

VON EULER, ULF (STOCKHOLM). **Adrenalin in Fever.**

Paleness, hyperglucemia, increased metabolism, and rise of temperature are known as some of the general clinical symptoms in fever. These symptoms also occur after injection of adrenalin. For this reason the author made an investigation in order to determine if adrenalin was produced during fever. In 1924 Osawa showed that tuberculous blood possessed a vaso-constrictor effect on frog's vessels. In 1926 the author stated that this effect occurs with all sorts of fever blood. In order to prove that this vaso-constrictor effect was due to adrenalin, Thunberg's methylene-blue method was used in the way described by Ahlgren. In the evacuated system of minced frog's muscle or rabbit's muscle and methylene-blue, with potassium phosphate as a buffer, the spontaneous oxidation-reduction was studied after addition of serum in various concentrations. Normal human serum shortened the time of decoloration, *i.e.*, activated the oxidation, in concentrations between 1:6 and 1:400. Serum, which was taken from patients with fever or from rabbits after heat-puncture, stimulated the oxidation in the system mentioned above in concentrations as low as 1:6400-1:25000. The same effect occurred after injection of adrenalin in man or when adrenalin was added to serum directly. This effect in connection with the sensitiveness against alkaline reaction, and the antagonism against insulin and glucose is, as Ahlgren stated, characteristic for adrenalin.

The loss of the ability to get fever after adrenalectomy, which is true also for the effect of the heat-puncture (Liljestrand and Frumerie), the reactions of the adrenal glands in longlasting fevers in connection with the statements made above support the assumption that adrenalin plays a very important rôle in fever.

VON EULER, U. and G. LILJESTRAND (STOCKHOLM). **An Effect of Muscular Work on Human Blood Serum.**

The velocity with which methylene blue *in vacuo* is reduced by minced muscle according to the method of Thunberg as modified by Ahlgren affords a possibility of determining the presence of minute quantities of certain highly active substances, among others some hormones, as demonstrated by v. Euler for serum in fever.

During rest blood serum of normal man accelerates the reduction of methylene blue by frog's muscle in a concentration as low as about 1:400. During muscular work we found a very considerable increase of this accelerator effect. Thus after rather heavy work (756 kgm. per min. during 10 min.) an acceleration was established even in a concentration of 1:12,000. The effect increases with the amount of work per minute and to a certain extent also in proportion to the total work performed.

This effect of blood serum is not diminished if air is bubbled through the serum at 37° for 4 hours, nor if the serum is made slightly alkaline. It is thus not adrenaline. The fact that choline is continually eliminated by the urine and has recently (Klee and Petropoliades) been found there in increased quantities after heavy muscular exercise made it desirable to obtain information whether the effect found could be attributed to choline. It was found that choline gives an acceleration of the reduction of methylene blue in a concentration as low as about 10^{-11} . The maximum effect was obtained at about 10^{-10} . This effect could be entirely abolished by atropine 10^{-10} to 10^{-7} . Also the increased accelerator effect of serum in muscular exercise was completely inhibited by atropine 10^{-4} . Histamine, however, which also increases the reduction rate of methylene blue considerably, was not antagonized by atropine.

So far our results are thus in harmony with the assumption that the effect found is mainly due to choline.

EVANS, HERBERT M. and SAMUEL LEPKOVSKY (BERKELEY). **On Some Relations of Vitamin B to Fat and Carbohydrate Metabolism.**

On a diet of sucrose and casein, more antineuritic B is necessary for growth than with other diets known to us. Replacing the sucrose with only 10 per cent of fat always lowers the vitamin B requirements. When 50 per cent fat is present, animals live at least six months without signs of beri-beri.

Direct evidence that antineuritic vitamin B is related to carbohydrate metabolism, at least in advanced stages of the deficiency, particularly when the animals show symptoms of beri-beri, has been obtained from glucose tolerance studies. Low B animals show reduced tolerance for glucose whereas controls, similarly treated and of the same weight, show excellent tolerance.

EYSTER, J. A. E. and WALTER J. MEEK (MADISON). **Venous Pressure.**

The effects of various procedures on the venous pressure in the experimental animal (dog) have been studied. Venous pressures, along with arterial pressure and respiration, have been recorded simultaneously from the right auricle, the iliac vein and the external jugular vein.

The most important result appears to be the relative independence of venous and arterial pressures. Extensive changes produced in the latter by the injection of adrenalin, stimulation of the central end of the vagus

nerve, occlusion of the descending aorta and by other procedures, affect venous pressures to a limited degree only. The pressure in the auricle tends to rise slightly or moderately, while iliac and femoral pressures are little if at all affected. Marked diminution in cardiac output by peripheral vagus stimulation produces a moderate rise in auricular pressures, but slight and inconstant effects on the venous pressures in the iliac and jugular veins.

The results support the view of the comparative stability of venous pressures under approximately normal conditions and the limitation of pressure changes transmitted from the arterial system, due probably to the fact that the peripheral vascular bed may vary its capacity through wide limits.

FABRE, RENÉ (PARIS). Contribution à l'étude des stérols de levure.

M. Fabre expose les résultats qu'il a obtenus dans l'étude des stérols de levure: séparation des stérols droit et gauche; propriétés physiques et chimiques du zymostérol; étude biologique.

La levure de bière contient au moins deux stérols: l'*ergostérol* levogyre et le *zymostérol* dextrogyre.

Entre les deux corps, il existe non pas une simple dissemblance d'ordre stéréochimique, mais une différence plus profonde de constitution moléculaire, la formule du zymostérol concordant avec celle d'un oxyergostérol.

Les propriétés absorbantes du zymostérol dans l'ultraviolet sont beaucoup plus faibles que celles de l'*ergostérol*; on n'observe aucun maximum caractéristique dans la région 2700-3000 U.A. L'irradiation n'apporte aucune modification à la courbe d'absorption.

La réaction photochimique conduit à un produit très faiblement antirachitique, à moins que des traces d'*ergostérol* entraînées malgré tous les soins apportés au fractionnement et non décelables à l'examen optique les plus minutieux, soient suffisantes pour expliquer la valeur biologique du zymostérol irradié que nous avons étudié.

FARKAS, G. (BUDAPEST). Untersuchungen über den Energieumsatz und die Ernährung landwirtschaftlicher Arbeiter.

Der Zweck unserer Versuche war den Energieumsatz bei landwirtschaftlicher Arbeit direkt, an Ort und Stelle zu bestimmen. Die Untersuchungen wurden während der Erntesaison mit der Douglas' schen Sackmethode an mehreren landwirtschaftlichen Arbeitern ausgeführt. Zuerst bestimmten wir die Grösse des täglichen Energieverbrauches und nachher die Ernährungsverhältnisse bei freigewählter Kost. Fernerhin führten wir Untersuchungen aus, in welchen die Arbeiter eine Kost von bekannten kalorimetrischen Werte erhielten. Diese Kost entsprach dem täglichen Energie-Bedarfe. Da die ergometrische Bestimmung der äusseren Arbeit, der einzelnen Arbeitsformen und die Berechnung der Arbeit in Meterkilogrammen aus diesen Werten nicht ausführbar war, zerteilten wir die Erntearbeit in einzelne Komponenten und durchführten den Respirationsversuch bei jeder Komponente womöglich 50-mal, um daraus gute Mittelwerte zu erhalten. Durch Summation der einzelnen Perioden, die quasi als Momentaufnahmen dienten, versuchten wir den täglichen Energieverbrauch zu bestimmen.

Dies geschah in zweifacher Weise. Erstens wurde der Energieumsatz der einzelnen Arbeitsformen in der Zeiteinheit bestimmt und diesen Wert

multiplizierten wir mit den täglichen Arbeitsstunden. Wie voraus zu sehen war, sind diese Werte höher als die wirkliche Arbeitsgrösse, da der Arbeiter mit kleineren Unterbrechungen arbeitet. Diese Unterbrechungen konnten wir nicht ganz genau bestimmen. Mit dieser Methode berechneten wir den täglichen Energieumsatz zu 6974 kg. Kal.

Mit einer anderen Rechnungsmethode bestimmten wir die Tagesleistung; die Wärmeproduction wurde einestheils bei den einzelnen Arbeitsformen z. B. beim Abmähen einer qm-Oberfläche, Einbinden einer Garbe u. s. w., bestimmt anderenteils stellten wir die Tagesleistung fest und erhielten durch Multiplikation den' der Tagesleistung entsprechenden Energieumsatz. Mit dieser Methode ergab sich der tägliche Energieumsatz für 5667 kg.Kal., welcher Wert um 20 Procent niedriger ist als Ersterer.

Auf den Grundumsatz wurde in beiden Fällen Rücksicht genommen.

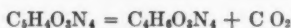
Neben dem Energieumsatz wurde auch die Nahrungsaufnahme der an freigewählter Kost lebenden Arbeitern festgestellt, welche täglich 4056 kg.Kal. entsprach. Aus diesen Daten kann die, während der drei Wochen lang dauernden Arbeitsperiode entstandene Gewichtsabnahme erklärt werden. In jenen Fällen in welchen der tägliche Energiebedarf mit 6000 kg.Kal. gedeckt wurde blieb die Gewichtsabnahme aus, fernerhin konnte Fett, Kohlehydrat—Gleichgewicht und Stickstoffretention erzielt werden.

FAURÉ-FERMIET, E. (PARIS). Un film cinématographique représentant les amibocytes des Invertébrés sous leur forme active de choanoleucocytes et montrant les mouvements de leurs membranes hyaloplasmiques.

FAURÉ-FREMIET, E. (PARIS). Démonstration microscopique sur les caractères physiques de ces minces lames hyaloplasmiques observées par réflexion.

FELIX, K. und W. SCHULER (MÜNCHEN). Die Urikolyse.

Beim fermentativen Abbau der Harnsäure entsteht Allantoin und Kohlensäure.



Die Endprodukte der Reaktion enthalten zwei Atome Wasserstoff und zwei Atome Sauerstoff mehr als die Harnsäure. Intermediär werden ein Atom Sauerstoff und ein Molekül Wasser aufgenommen. Nach der Gleichung setzt sich der Gesamtvorgang der Urikolyse aus drei Teilvorgängen zusammen: 1. einer Hydrolyse, 2. einer Oxydation und 3. einer Kohlensäureabspaltung. A priori ist es nicht wahrscheinlich, daß diese Vorgänge durch ein und dasselbe Ferment, die sogenannte Urikase geleitet werden. Dazu ist im allgemeinen die Spezifität der Fermente zu streng begrenzt.

Die Bestimmung des pH-Optimums für den Abbau der Harnsäure ergab zwei ausgezeichnete Punkte, den einen bei pH 8,9 und den zweiten bei 9,9-10, während für die Bildung von Kohlensäure nur ein Optimum besteht, das mit dem zweiten Optimum des Harnsäureabbaus zusammen fällt. Im ersten Optimum des Harnsäureabbaus wird nur wenig, etwa ein Fünftel der aus der abgebauten Harnsäure berechneten Kohlensäure gebildet, im zweiten dagegen die gesamte Menge. Indem man erst die

Harnsäure beim ersten Optimum vollständig oxydieren und dann bei pH 9,9 das Ferment weiter wirken läßt, kann man die Urikolyse in zwei Phasen zerlegen. Beide Phasen sind Fermentreaktionen. Bei der zeitlichen Trennung der beiden Phasen ergibt sich für die Abspaltung der Kohlensäure in der zweiten Phase das gleiche Optimum wie bei der Einwirkung des Leberpulvers auf die Harnsäure selbst.

In der ersten Phase wird auf ein Molekül Harnsäure genau ein Atom Sauerstoff verbraucht. Die Hydrolyse fällt ebenfalls in die erste Phase, erfolgt aber etwas später als die Oxydation. Es wird eine Aminogruppe frei, also nur ein Molekül Wasser eingelagert und nur ein Ring, wahrscheinlich zwischen 1 und 6, geöffnet. Durch Oxydation und Hydrolyse entsteht in der ersten Phase aus der Harnsäure ein Zwischenprodukt, das einen Harnstoffrest als freie Seitenkette trägt. Es spaltet sehr leicht ein Molekül Harnstoff ab und ist wahrscheinlich ein Ureid der Alloxansäure. Von dem Zwischenprodukt aus öffnen sich zwei Wege. Der biologische führt zu Allantoin und Kohlensäure und der chemische zu Harnstoff und Alloxansäure.

Als Fermentpräparate dienen Trockenpulver und Extrakte von Schweineleber. Die Urikase besteht aus mindestens zwei wahrscheinlich aber drei Teilfermenten.

FENN, W. O. (ROCHESTER, NEW YORK). **Mechanical Energy Expenditure in Sprint Running as Measured by Moving Pictures.**

The results are summarized in the following table:

Total, from excess oxygen.....	13.0 horse power
Production of kinetic energy in arms and legs.....	1.67
Checking arms and legs (probable estimate).....	0.67
Gravity.....	0.10
Wind resistance.....	0.13
Contact of foot with ground.....	0.37
Total mechanical energy.....	2.94 or 22.6% of total

The kinetic energy of the limbs was calculated for every 0.033 second interval during 22 different sprints from measurements on moving picture films. The exposures were made at a rate of 120 per second. The kinetic energy of each part (in relation to the body) is plotted against time. The sum of all the increases in kinetic energy observed during one cycle divided by the length of the cycle gives the average value 1.67 horse power. It is reasonable to estimate 0.4 of this amount to check these movements. Variations in the positions of the center of gravity of the body due to the varying positions of the limbs have been calculated. The rate of working against gravity is thus determined. An apparatus is built with which the horizontal forward and backward components of the foot pressure on the ground have been recorded as function of time. Subjects so far available have all pushed themselves backwards slightly when the foot touches the ground. This rate of energy loss amounts to 0.5 horse power of which 0.13 may be taken as the wind resistance.

The results indicate that 22.6 per cent of the total chemical energy is developed as mechanical energy. This is developed *in spite of muscle viscosity and in addition to such frictional loss*. If the initial heat is 40 per cent then the fraction left for viscosity is 17.4 per cent. The estimates of mechanical energy expenditure may be slightly too high

(10-15 per cent) because of energy transfer from one limb to another. They are too low because sideways movements have been neglected. One factor limiting speed of bodily movements is the inability to maintain tension in a rapidly shortening muscle. This inability may be due to delay in an energy-giving chemical reaction as well as to viscous delay in the external manifestation of tension. A more important limiting factor is the rapidly increasing force necessary to accelerate the limbs at high speeds.

FERRY, RONALD M. and A. M. PAPPENHEIMER, JR. (BOSTON). **Studies in the Chemistry of Hemoglobin. IV. The Equilibrium Between Oxygen and the Hemoglobin of Sheep in Whole Blood.**

Adair¹ has proposed a theory explaining the equilibrium between oxygen and hemoglobin based on the assumption that hemoglobin takes up oxygen in steps to form Hb_4O_2 , Hb_4O_4 , Hb_4O_6 , and Hb_4O_8 , where Hb_4 denotes a molecule of reduced hemoglobin having the molecular weight 66,800. This assumption lacks direct experimental support. None the less Ferry and Green² have shown that the behavior of oxygen and recrystallized horse hemoglobin in buffered solutions at 25°C. is at least empirically described in terms of this theory according to the equation:

$$\text{Per cent saturation} = 100 \times \frac{0.25(K_1[O_2]) + 0.16(K_1[O_2])^2 + 0.192(K_1[O_2])^3 + 2.7(K_1[O_2])^4}{1 + (K_1[O_2]) + 0.32(K_1[O_2])^2 + 0.256(K_1[O_2])^3 + 2.7(K_1[O_2])^4}$$

They were further able to show that K_1 was a function of hydrogen ion concentration having the form

$$K_1 = \frac{K'_A [H^+]^2 + K'_S K'_R}{K'_R + [H^+]^2}$$

over the range pH 6.55 to 8.89. Where

$$K'_A = \frac{[H_2Hb_4][O_2]}{[H_2Hb_4O_2]}, K'_S = \frac{[B_2Hb_4][O_2]}{[B_2Hb_4O_2]}, K'_R = \frac{[H^+]^2 [Hb_4]}{[H_2Hb_4]}$$

In the case of oxygen in equilibrium with hemoglobin in whole sheep's blood at 37.5°, we have been able to show that data recently obtained by Henderson, Dill, Bock, and Talbot³ may be described equally well in terms of equations having the same general form over a similar pH range. The numerical values of the constants are, of course, different. They are compared with those for crystalline horse hemoglobin solutions in the following table:

	K'_A	K'_S	K'_R	$\sqrt{K'_R}$
Crystalline horse hemoglobin.....	0.045	0.345	2.50×10^{-16}	1.58×10^{-8}
Hemoglobin in whole sheep's blood..	0.012	0.056	12.1×10^{-16}	3.48×10^{-8}

It is thus possible, quantitatively, to describe differences in the physiological behavior of the blood of horse and sheep at 25° and 37.5°C respectively in terms of constants having physiochemical significance.

¹ G. S. Adair. Journ. Biol. Chem., 1925, lxiii, 529.

² R. M. Ferry, and A. A. Green. Journ. Biol. Chem., 1929, lxxxix, 175.

³ L. J. Henderson, D. B. Dill, A. V. Bock and J. Talbot. Personal communication.

FEUILLIÉ, EMILE (PARIS). Moelle osseuse et hématopoïèse.

Les conceptions actuelles au sujet de l'hématopoïèse dérivent surtout de l'expérimentation sur le lapin. A la suite de saignées répétées ou d'injections intra-veineuses de toxiques ou de microbes à des lapins de plus de 3 kilos (la saignée produisant une dyscrasie comparable à une intoxication) si on sacrifie l'animal après 48 heures on voit que la moelle osseuse primitivement grasseuse est devenue rouge. On y trouve tous les éléments décrits par les classiques.

Mais ce qui a toujours manqué dans ces expériences, c'est une bonne interprétation du processus. En effet: en multipliant les expériences et en sacrifiant des animaux à la 6^{me}, 12^{me}, 18^{me}, 24^{me} et 30^{me} heure, on constate qu'il ne s'agit nullement d'une reviviscence de la moelle osseuse. Ce qui s'est produit, c'est de la congestion souvent hémorragique, avec diapédèse des divers éléments du sang circulant. Beaucoup de mononucléaires à noyau pâle ayant des granulations dans leur protoplasme ne sont que des polynucléaires en pérévolution décadente dont le noyau a fait retour à l'état mono. La véritable cellule mère est le lymphocyte venu du sang qui se transforme in situ en cellule mononucléée à protoplasme basophile et en globule rouge à noyau. La moelle osseuse n'est donc pas un organe hématopoïétique.

Il est facile de se rendre compte aussi que le centre clair du follicule lymphatique n'est pas un lieu de leucopoïèse, mais un champ de bataille où tout n'est que dégénérescence ou pérévolution décadente. La cellule de Flemming provient du lymphocyte. Les karyokinèses sont des mitoses dégénératives en panne.

L'organe hématopoïétique est le tissu lympho-conjonctif.

On arrive ainsi à l'unicisme intégral.

FISCHER, E. (FRANKFURT A.M.). Die Wärmebildung des isolierten Säugetiermuskels.

Unter geeigneten Versuchsbedingungen gelingt es, isolierte Säugetiermuskeln (Maus) unter Erhaltung normaler Erregbarkeit hinreichend lang überleben zu lassen und mit Hilfe der Hill-Hartree'schen thermoelektrischen Methode die Wärmebildung nach Einzelreiz und tetanischem Reiz

zu bestimmen. Für den isometrischen Quotienten $\frac{\text{Wärme}}{\text{Spannung} \times \text{Länge}}$ des Warmblütermuskels gilt, abgesehen von kurzen Reizen, die gleiche Gesetzmässigkeit wie für den des Kaltblütermuskels, d.h. für Reize von mehr als ca. 0,15 Sekunden Dauer erfährt der isometrische Quotient Erhöhungen, die proportional mit der Reizdauer anwachsen. Für Reizzeiten vom Einzelreiz bis zu einem Tetanus von ca. 0,15 Sek. erweist sich der isometrische Quotient als unabhängig von der Reizdauer, aber als abhängig von dem Betrag der entwickelten Spannung, derart dass grössere Spannungsentwicklung, also längere Reizdauer, eine Abnahme des isometrischen Quotienten bedingt. Infolge dieser beiden Gesetzmässigkeiten besitzt der isometrische Quotient für tetanische Reize von ca. 0,1 Sek. Dauer einen Minimalwert, d.h. bei einem solchen Reiz findet optimale Energieausnützung statt. Der Energieaufwand bei einem Tetanus von kurzer Dauer ist pro Spannungseinheit für den Warmblüter deutlich niedriger als beim Kaltblüter, während für längere Tetani der Warmblüter zur Aufrechterhaltung der Spannung einen Energieaufwand

benötigt, der dem des Kaltblütermuskels bei der gleichen Temperatur (38°C) entsprechen würde. Auch beim Warmblütermuskel zerfällt die initiale Wärmebildung in drei Phasen (Wärme während der Spannungsentwicklung, Wärme während der Aufrechterhaltung der Spannung, Erschlaffungswärme). Die Bildung der Erholungswärme setzt beim Warmblüter viel früher und schneller ein als beim Kaltblüter und kommt dementsprechend auch rascher zu ihrem Abschluss als bei letzterem. Während beim Kaltblüter die Erholungswärme etwas grösser als die initiale Wärme ist, so scheint beim Warmblüter die Erholungswärme etwas hinter dem Ausmass der initialen Wärme zurückzubleiben.

FISCHER-WASELS, BERNH. (FRANKFURT A.M.). Grundlagen der allgemeinen Geschwulstdispositionen.

Notwendig zur Entstehung einer Geschwulst sind stets zwei Faktoren: Die Geschwulstkeimanlage und die Geschwulstdisposition des Gesamtkörpers. Beide Faktoren können sowohl embryonal gegeben, ererbt sein, als auch postembryonal erworben sein. Hierfür werden die experimentellen Beweise beigebracht.

Die Versuche, morphologische Grundlagen der allgemeinen Geschwulstdisposition aufzufinden, sind bisher gescheitert. Wir haben daher nach physiologischen Grundlagen gesucht und zunächst die Verhältnisse der Atmung und Gärung des Gesamtkörpers bei der Geschwulstdisposition bearbeitet. Diese Untersuchungen sind von meinem Assistenten Dr. W. Büngeler ausgeführt worden. Es fanden sich in Haut, Leber und Niere von Tieren, die durch chronische allgemeine Teer- oder Arsenvergiftung in das Stadium der Geschwulstdisposition gebracht worden waren eine Herabsetzung der Oxydationsvorgänge und eine Steigerung der Glykolyse. Dieselben typischen Veränderungen an den genannten Organen wurden bei Mäusen mit Spontantumoren gefunden, soweit uns solche bisher zur Verfügung standen. Bei transplantierten Geschwülsten (Sarkom und Carcinom der Maus) fanden sich diese Veränderungen nicht, dagegen andere, die durchaus denen entsprachen, wie wir sie bei parentaler Eiweissinjektion nachweisen konnten. Die hierbei wechselnden Befunde konnten durch gleichzeitige histologische Untersuchung aufgeklärt werden.

FLEISCH, A. (DORPAT, ESTLAND). Bahnung und Hemmung der proprioceptiven Atmungsreflexe durch die Atmungsphase.

Durch geringe aber rasch erfolgende Widerstandsänderung in der Strombahn der Respirationsluft erfährt die Atmungsmuskulatur Spannungsänderungen, die mit proprioceptiven Atmungsreflexen beantwortet werden. Meistens handelt es sich um kompensierende Reflexe, die der stattgehabten Störung entgegenwirken, z.T. aber auch um adaptierende, die der Störung nachgeben. Ausserdem treten Rückschlagsreflexe auf. Bei Mensch und Tier treten dieselben Reflexe auf und sie sind auch von ähnlicher Intensität.

Die Stärke jedes einzelnen Reflexes (= Prozentsatz der durch den Reflex rückgängig gemachten Störung der Luftstromgeschwindigkeit) ist weitgehend unabhängig von der Reizstärke, aber sehr stark abhängig von der Atemphase. Im Beginn der Inspiration hat der inspirationsaktivierende Reflex sein Maximum und nimmt gegen das Ende der Inspiration hin

sukzessive ab, der inspirationshemmende Reflex hingegen hat im Beginn der Inspiration sein Minimum, um gegen Ende der Inspiration in seine maximale Stärke überzugehen. Ähnlich verhält es sich mit dem expirationsaktivierenden und dem expirationshemmenden Reflex während der Expiration. Der quantitative Ablauf der Reflexdispositionen des Atmungszentrums während einer Atmungsphase wird graphisch dargestellt. Es werden Anhaltspunkte gewonnen über den quantitativen Erfolg der Superposition von 2 Reflexen.

FLORKIN, MARCEL¹ (LIÈGE). L'action bathmotrope des nerfs autonomes et des substances autonomomimétiques sur les organes à musculature lisse.

La faradisation du splanchnique allonge la chronaxie de l'estomac (crapaud). L'adrénaline allonge la chronaxie du rectum isolé (grenouille).

La faradisation du vague réduit la chronaxie de l'estomac (grenouille). Les substances à action parasymphathico-mimétique réduisent la chronaxie du rectum isolé (grenouille).

Ces faits sont à rapprocher de ce qui se passe au niveau du coeur. La faradisation du sympathique allonge en effet la chronaxie du myocarde (Henri Fredericq) et c'est dans le même sens qu'agit l'adrénaline (Henri Fredericq).

La faradisation du vague réduit la chronaxie du myocarde (Henri Fredericq, M. Lapique et C. Veil, Field et Brücke) et les substances parasymphathico-mimétiques exercent la même action (Henri Fredericq, C. Veil).

De l'ensemble de ces faits on tire les conclusions suivantes:

(1) Le splanchnique et le vague ont une action bathmotrope sur l'estomac.

(2) Le sens de l'effet bathmotrope de la faradisation des nerfs sympathiques, apprécié par la mesure de la chronaxie, est le même (positif) au niveau du coeur et au niveau de l'estomac. Pour les nerfs parasymphathiques le sens de l'effet bathmotrope est aussi le même (négatif) au niveau des deux organes.

(3) Les substances sympathico-mimétiques et les substances parasymphathico-mimétiques exercent la même action bathmotrope que les nerfs correspondants. Pour chacune des deux catégories, qui agissent en sens inverse, l'effet bathmotrope est le même au niveau du coeur et au niveau du rectum.

FOLIN, OTTO (BOSTON) and HAGVIN MALMOS (LUND). Improved Micro Method for the Determination of Blood Sugar. (Demonstration)

FÖLLING, A. (OSLO). On the Site of the Ammonia Production in Man.

Using the method of Rehberg for the determination of the filtration rate of the kidneys, the amount of ammonia in the blood filtrate was determined, and at the same time the ammonia actually formed in the urine.

In acid urine the ammonia content of the urine was always higher than the ammonia filtered from the blood. The conclusion is drawn that most of the urinary ammonia must have been formed in the kidneys. At a

¹ Fellow of the C. R. B. Ed. Foundation.

certain rather low grade of alkalinity of the urine this production of ammonia ceases.

The investigations will be published in full in *Acta Medica Scandinavica* for this year.

FORBES, A. and H. DAVIS (BOSTON). **Apparatus Used in Electro-Physiological Research. (Demonstration)**

FORBES, E. B. (STATE COLLEGE, PENNSYLVANIA). **The Problem of Determination of Net-Energy Values of Feeding Stuffs.**

The determination of net-energy values implies the presence of protein, mineral nutrients, and vitamins, in optimum quantities, and due consideration of the fact that the heat production varies, as related to the plane of nutrition in a manner expressed by a reversed or S curve.

The fasting katabolism, as the base value of heat production, and as the measure of the maintenance requirement of net energy, is standardized as the heat production of the first day following the attainment of a status of metabolism characterized by the non-protein respiratory quotient of fat.

The heat production of fast being considered as including two factors, a waste heat of utilization of body nutrients katabolized, and a theoretical, minimum, base value, including no such waste,—the curvature of the line of heat production in relation to increasing food consumption is interpreted as resulting from 1, the increasing concentration of metabolites circulating in the blood; 2, the change in the proportions of protein, fat, and carbohydrate katabolized,—with increase in the katabolism of food nutrients and decrease in the katabolism of body nutrients; 3, the energy expense of synthesis of body nutrients (fat from carbohydrates), and 4, the decreased metabolizability of the food at the higher planes of nutrition.

A system of net-energy values must recognize the distinctly greater economy of utilization of food energy for maintenance than for body increase. Net energy for milk production seems to be the same as for maintenance.

The most difficult unsolved problem in net-energy determination is the separation of the net-energy of grain and roughage (hay), since such feeds cannot be fed separately, at practical levels of production, and since combining the two changes the rate of economy at which they are utilized.

FOULGER, J. H. and D. E. JACKSON (CINCINNATI). **The Pharmacological Action of Organic Barium Compounds.**

According to the method of Pfeiffer and Modelski (*Zeitschr. physiol. Chem.*, lxxxi, 329, 1912) one of us (F.) has prepared glycine-barium chloride $(\text{NH}_2\cdot\text{CH}_2\cdot\text{COOH})_2\cdot\text{BaCl}_2\cdot\text{H}_2\text{O}$ with which these experiments have been primarily concerned. We find that this organic combination of barium has a somewhat different and milder action than does pure barium chloride.

Small doses (3 cc. to 5 cc. of 0.1 per cent) intravenously in medium sized dogs produce a small rise in arterial pressure which is maintained for twenty or thirty minutes in favorable cases. The respiration is entirely uninfluenced.

With repeated, or larger, doses there is very regularly produced a striking series of extra ventricular systoles which give a perfectly regular series of beats having an amplitude of one half to one and one-half inches in height as recorded on the kymograph with a mercury manometer connected with

the carotid artery. These series of extra systoles develop suddenly after injection of adequate doses of the drug and last for varying lengths of time, from a few seconds up to twenty minutes or longer (with larger doses).

We have found that these extra systolic series can be stopped at once and the normal beat restored by a number of drugs which act in very different ways.

First: drugs which lower blood pressure, as sodium nitrite and boldine, may check the extra systoles and restore the normal rhythm, but these drugs are much less certain in their action than are solutions of sulphates of which sodium sulphate is perhaps the best, although we have checked the extra beats with magnesium and with sodium ethyl sulphate. This action would appear to depend on the formation of a combination between the barium and the sulphate radicles in the tissues of the heart itself.

Secondly: atropine may check the extra systoles and at once restore the normal beats, this action perhaps depending on vagus paralysis and possibly on some obscure stimulation of the cardiac muscle.

Thirdly: epinephrin is very effective in checking extra systoles and restoring the normal rhythm.

After all these counteracting drugs it is usually possible to bring on a number of series of extra systoles by repeating the injections of the glycine-barium compound.

Lastly: quinidine acts strongly to check the extra systoles and this effect is very lasting on the heart muscle, moderate doses of quinidine often serving to prevent any further development of extra systoles by later doses of the barium compound.

FRANK, OTTO (MÜNCHEN). Methoden zur Bestimmung der Blutgeschwindigkeit

Auf Grund der von mir wiederholt entwickelten Prinzipien habe ich konstruiert:

- 1.) Ein optisches Differentialmanometer
- 2.) Ein optisches Strompendel
- 3.) Eine optische Stromuhr

Die Typen der Konstruktionen werden demonstriert. Jede hat ihre besonderen Verwendungsmöglichkeiten. Einige mit ihnen gewonnene Ergebnisse werden mitgeteilt.

FREDERICQ, HENRI (LIÈGE). L'action bathmotrope des nerfs viscéraux: effets de la faradisation subliminaire du plexus splénique sur la chronaxie propre de la rate.

La chronaxie propre de la rate d'un chien anesthésié par la morphine et l'éther est mesurée par la méthode des fermetures de courant constant. La rate réagit, on le sait, par une contraction à chaque fermeture du courant. Le seuil de la contraction splénique est observé par l'intermédiaire d'un oncographe splénique qui transmet ses mouvements à un manomètre à eau. On sait, d'autre part, que la faradisation des branches nerveuses périphériques du plexus splénique détermine également une contraction de la rate.

Si on procède à cette faradisation en employant une intensité située immédiatement sous le seuil, on peut observer que le nerf splénique exerce une action très nette sur l'excitabilité propre de la rate: la chronaxie de cet organe est nettement diminuée; la réaction est réversible et l'expérience

peut être recommencée avec une sécurité absolue un nombre indéfini de fois. Par contre, la rhéobase de la rate ne montre aucune variation systématique pendant la faradisation du nerf splénique.

Ces résultats étendent à un nouveau système neuro-viscéral la notion d'action bathmotrope signalée antérieurement à propos des nerfs régulateurs du cœur et des nerfs régulateurs du tractus digestif: rappelons en effet que le pneumogastrique cardiaque réduit la chronaxie des extrasystoles provoquées; cet effet a été observé chez le chien, la tortue et la grenouille par Henri Fredericq, M. Lapique et C. Veil, Field et Brücke; chez les poissons par Henri Fredericq et Adèle Brouha; et chez le poulpe par Henri Fredericq. Chez le chien, la faradisation de l'anneau de Viussens allonge au contraire la chronaxie cardiaque (Henri Fredericq). La faradisation du pneumogastrique diminue également la chronaxie de l'estomac de la grenouille, tandis que la faradisation du splanchnique allonge la chronaxie de l'estomac du crapaud (Marcel Florkin).

L'action bathmotrope exercée sur les organes viscéraux par les systèmes sympathique et parasympathique apparaît donc comme une action très générale; mais, il n'est pas possible de conclure que la chronaxie de ces organes est toujours réduite par le vague et toujours allongée par le sympathique, pas plus qu'on ne peut établir de corrélation entre le sens de la variation de la chronaxie de l'organe d'exécution et le rôle moteur (éventuellement accélérateur) ou modérateur des nerfs de la vie végétative. Mais une systématisation deviendrait possible si on pouvait considérer le nerf splénique comme une branche du système parasympathique. Il existe en faveur de cette opinion certains arguments (pharmacodynamiques) de probabilité.

FREDERICQ, LÉON (LIÈGE). Les différentes formes de la contraction du myocarde.

Le myocarde ventriculaire peut présenter les différentes formes suivantes de contraction:

Forme I.—*Contraction ordinaire de la pulsation (Systole normale)*, présentant une phase initiale A de raccourcissement rapide, se continuant en une phase de contracture B (plateau systolique). C'est une forme de contraction myogène, propre au myocarde et qu'on ne peut assimiler ni à une secousse simple, ni au tétanos des muscles du squelette. Phénomène électrique complexe: QRST d'Einthoven.

Forme II.—*Contraction brève (Systole avortée)*, semblable à la première phase A de la forme I. Elle se substitue à la forme I, quand le myocarde est mal nourri, par exemple, par arrêt de la circulation. Phénomène électrique simplifié: QR. Suppression de l'ondulation ST.

Forme III.—*Pouls alternant (Systoles alternativement fortes et faibles)*. Dans certains cas, il semble qu'il y ait, non une forme spéciale III de contraction, mais une simple alternance de contractions des types I et II.

Forme IV.—*Contraction idiomusculaire*. Contraction locale, persistante, tonique, provoquée par une excitation mécanique locale de la surface du cœur.

Forme V.—*Fibrillation ordinaire (Délire du cœur)*, que j'appelle *macrofibrillation* pour la distinguer de la forme VI. Rentre peut-être dans la forme I.

Forme VI.—*Microfibrillation*. Contractions incoordonnées des plus petits éléments du cœur. Se voit très bien, même à l'œil nu, sous forme de

tremblement lumineux, si l'on examine une surface de section d'un coeur de chien qu'on vient de sacrifier et qu'on éclaire vivement (lumière du soleil ou éclairage électrique). (Éventuellement démonstration de la microfibrillation.)

Les formes III et V rentrent peut-être dans les formes I et II. II n'y aurait alors que les formes I, II, IV et VI à considérer comme réellement distinctes.

VON FREY, M. (WÜRZBURG). **Zur Theorie der Temperaturempfindung.**

Bei starker Kühlung einer Hautfläche überdauert die Kaltempfindung für längere Zeit den Reiz. Nach der Theorie von E. H. Weber sollte dagegen mit dem Ende der Kühlung eine Wärmempfindung einsetzen. Das Erwartete tritt in der Tat auf, wenn man die Kühlung vornimmt an einer Hautstelle, die einen oder mehrere Wärmepunkte aufweist und wenn man durch den von K. G. Holm angegebenen Schutzring dafür sorgt, dass der Wärmeentzug nicht auf die Umgebung der Reizstelle übergreift. Der Versuch steht also nicht im Widerspruch mit der Theorie von Weber, er macht aber die von E. Hering vorgeschlagene Modifikation derselben unnötig.

VON FRIEDRICH, LADISLAUS (BUDAPEST). **Einwirkung von verschiedenen intraduodenal applizierten Reizen auf die Gallenwege.**

Es herrscht ein langer Streit in der Literatur darüber, ob eine Entleerung der Gallenblase oder eine veränderte Ausscheidung von Lebergalle nach intraduodenal einverleibten Substanzen erfolgt. Bevor man aber diese Frage prüft, zeigt es sich zweckmässig ganz prinzipielle Gesichtspunkte festzulegen. Zweck meiner Untersuchungen, die den Anfangsteil der Lösung dieses ganzen Fragekomplexes bilden, war, diese bisher noch nicht untersuchten Probleme zu lösen. Die Untersuchungen wurden an gesunden Menschen vorgenommen: nach 12 stündigem Fasten. Folgende Fragen wurden geprüft:

I. Übt die Einführung der Duodenalsonde allein einen Reiz auf die Gallenblase oder Leber aus? Eindeutiges Resultat: sowohl Menge, wie Farbe, Konsistenz, Bilirubingehalt des Duodenalsaftes änderte sich nie in 1½ Stunden Versuchsdauer.

II. Kann die mechanische Reizung der Schleimhaut einen Reiz ausüben? Eine Doppelsonde wurde eingeführt, auf das Ende der einen Sonde kam ein aufblähbare Gummiballon im Umfang von 8 cm. Dieses Ende lag tiefer, neben ihm die gewöhnliche Olive. Nach Einführung in den absteigenden Ast wurde der Ballon von aussen aufgeblasen, dadurch wurde die Schleimhaut des Duodenums gereizt, der Abfluss des Duodenumsaftes nach aussen wurde stärker, aber eine Veränderung in Farbe, Vichorität, Bilirubingehalt konnte nicht festgestellt werden.

III. Thermische Reize. Einspritzung von heissem Wasser oder Eiswasser rief nie eine Veränderung hervor.

IV. Die verschiedene Lage des Sonden Knopfes hat einen entschiedenen Einfluss auf die Gallenblasen-Entleerung. Röntgenologisch sowie bei den vorigen Versuchen auch, wurde festgestellt, wo die Olive der Duodenalsonde liegt. Liegt sie im Pars horizont alis superior, so kommt es bei Auslösung des Meltzer-Lyon'schen Reflexes zu keiner dunkleren Verfärbung des Saftes, auch wenn sie im Pars inferior, oder gar in der Flexura

duodeno jejunalis liegt, wird der Reflex viel schwächer. Die richtige Lage ist in der Höhe der Papilla vaterii. Es gibt daher eine reflexogene optimale Zone, von wo aus man am besten auf die Gallenblase einwirken kann. Es ist daher zu fordern, dass eine röntgenologische Kontrolle der Olive bei Duod. Sondierung immer erfolge, denn sonst kommt man zu falschen Resultaten. In der Literatur beschriebene Verschiedenheiten der Gallenblasen Entleerungsreflexe können auf die Nichtbeachtung dieser Befunde beruhen, d.h. auf verschiedene Lage des Olivenkopfes.

FROLOFF, J. P. (MOSKAU). Die Merkmale der Typen höherer Nerventätigkeit und die Grenzen ihrer biologischen Beständigkeit.

1. Die Versuche nach der Methode bedingter Reflexe bieten die Möglichkeit Typen höherer Nerventätigkeit (Temperamente) vom frühen Alter (von ungefähr 6 Wochen ab) zu differenzieren, wobei diese Differenzierung ihre Bedeutung auch beim Eintritt der Reife beibehält.

2. Erwachsene Tiere unterscheiden sich von den jüngeren durch die grössere Vollkommenheit der wesentlichen Nervenprozesse insbesondere der Inhibition, was leicht mit Hilfe von Spezialtesten in Anlehnung an die Methode der bedingten Reflexe und Hemmungen festgestellt werden kann.

3. Tiere ein und desselben Wurfes lassen zwei Typen erkennen: a) mit vorherrschendem Erregungsprozess und b) mit vorherrschendem Inhibitionsprozess. Ausserdem trifft man mitunter (etwa 10 Prozent) einen Typus an, den man als einen Gleichgewichtstypus bezeichnen kann.

4. Verschiedene Typen unterscheiden sich durch verschiedene Beharrlichkeit, nicht nur im Falle des Erstehens von Situationen, die durch den Verlauf des üblichen Experimentes (Differentiation äusserer Reize, komplexe Synthesen u.a.), sondern auch bei Wirkung einiger biologischer und pathologischer Faktoren (dauernder Hunger, Infektionskrankheiten).

5. Bei vollständigem Hungern des Tieres im Laufe mehrerer Wochen, sowie bei partiellem—im Laufe mehrerer Monate tritt anfangs eine Schwächung des Hemmungsprozesses, später aber auch eine Störung des Erregungsprozesses (Verschwinden von bedingten Reflexen) ein.

6. Das Hungern verwischt die individuellen Unterschiede nicht, fördert im Gegenteil ihre Kundgebung. Der Unterschied ist so auffallend, dass der Hunger an sich als Test für die Kundgebung typischer Eigenarten des Tieres gelten kann.

7. Dasselbe beobachtet man bei der Erkrankung an Hundepest, wobei einige dem erregbaren Typus angehörende Individuen an einer besonderen "nervösen" Pestform erkranken. Nach der Genesung äussert das Tier Symptome chronischer Störung im Bereich der bedingten Reflexe und besonders der bedingten Hemmungen bei vollständiger Intaktheit und sogar bei einer Steigerung der unbedingten Reflexe.

8. Die bisher durchgeführten Experimente berechtigen zur Annahme des entgegengesetzten (Inhibition) Typus von grösserer biologischer Beständigkeit, was zweifellos in Zusammenhang mit Prozessen der Anpassung der jeweiligen Tierart an die Verhältnisse menschlicher Kultur steht.

9. In Bezug auf den Menschen gelten die erwähnten Regeln *mutatis mutandis*, namentlich bei der Schätzung von Kollektiven, insbesondere von Kinderkollektiven, jedoch mit dem Unterschied, dass die Proportion der Typen hier eine andere sein mag, in Abhängigkeit vom Urbanisationsgrade, von beruflicher Selektion u.a. Faktoren sozialer Ordnung.

FULTON, J. F. and F. D. INGRAHAM (OXFORD). **Emotional Disturbances Following Experimental Lesions of the Base of the Brain (Pre-Chiasmal).**

The investigation was undertaken in the belief that the frontal lobes give rise to tracts of fibres which pass, either directly, or mediately through the globus pallidus, to the centers in the hypothalamus. The existence of such tracts was suggested by the fact that pupillary changes are produced by faradic stimulation of a discrete point on the anterior pole of the frontal lobes (Karplus and Kreidel). A surgical procedure was evolved in order to sever this postulated pathway and thus to release the hypothalamus from the control exerted by the frontal lobes. After an extensive bilateral decompression the base of the brain was exposed adequately to make an incision in the brain 3 to 4 mm. anterior to the optic chiasm, 2 to 3 mm. in depth, and extending from the mid-line to the olfactory radiation.

A large number of healthy, friendly, playful cats was used, the period of survival after operation varying from 1 to 4 months. In each instance in which the lesions had been bilateral and accurately placed (extending to the mid-line) there was immediately a striking change in the disposition of the animal. Previously friendly and playful, they entered after operation into a state of chronic rage, *i.e.*, a condition in which signs of fury were much more easily elicited than in a normal animal. Gently stroking the back, for instance, would evoke spitting, scratching, and biting, accompanied by signs of diffuse discharge of the sympathetic nervous system (*e.g.*, dilatation of pupils, sweating, and pronounced pilo-motor response). We believe that this unusual state is due to a release of the hypothalamic centers from the control normally exerted by the frontal lobes. These observations appear to throw light upon the emotional disturbances and changes in behaviour seem clinically with lesions of the base of the brain.

FUNK, CASIMIR (PARIS). **The Sex Hormones.**

The male and female sex hormones, as indicated in our preliminary communications (with Harrow and Lejwa) show far reaching analogies in their chemical behavior. Both substances can be extracted from various sources by means of chloroform and are soluble in dilute alkalies. If one subjects crude extracts to the action of alkalies, the active substances are found in the non-saponifiable fraction. We are dealing here either with fatty acids, or, which is more likely, with phenols or alcohols. The sex hormones are a new class of chemical substances, resembling perhaps the new vitamin, brought in evidence by Evans and Burr in certain fats and oils. The lessened activity of the sex hormones in the form of their aqueous solutions suggests a separation into two constituents, one of which is less soluble, than the other.

FÜRTH, OTTO (VIENNA). **Oxidation of Several Body-Constituents by Activated Charcoal. (Experiments in Collaboration with Hans Kaunitz.)**

The well-known researches of Warburg have brought the subject of oxidation on carbon surfaces into the sphere of physiological interest. Our researches are founded on these experiments, as well as on those of Meyerhof, Bauer and Wunderly, Rideal and W. Mary Smith. We have especially studied the oxidation of amino acids, by boiling solutions of them under the reflux condenser in the presence of highly active charcoal. We especially studied the conversion of amino nitrogen into ammonia nitrogen, which sometimes was as much as 70 per cent of the total nitrogen involved.

We confirmed Warburg's view, that amino acids of higher molecular weight (such as leucine, phenylalanine and tyrosine) undergo more rapid conversion than those of lower molecular weight (alanine). It is interesting to note that the $-CO \cdot NH_2$ group (as for instance in acetamide, benzamide and asparagine) is not affected at all. There is not even a trace of hydrolysis. Further proteins (such as glutine and peptone) are hardly affected; the glycylglycine-linkage is therefore perfectly resistive to this oxidizing interference. The oxygen of *ring systems* (proline, histidine) is but poorly affected.

We found *sugar-carbon* scarcely less active than *carbo medicinalis* (Merck). From Warburg's point of view we may suppose, that even the minute traces of iron contained in the sugar-carbon seem to be sufficient to stimulate oxidation. Sugar-carbon prepared with *copper*, *manganese* or *vanadium* has been found to be less active. We were never able to convert the *total amount* of amino-N of an amino acid into ammonia-N. From carefully conducted experiments with alanine we learned that this deadstop in the reaction is due to the fact that some of the amino acid is simply withdrawn by absorption to the charcoal, whereby the latter agent becomes inactive.

Phenolic substances (phenol, pyrocatechol) are destroyed with surprising readiness.

Warburg knew that grape sugar is resistive to charcoal oxidation. But in our method of interaction we have observed that a triose—*dihydroxyacetone*—as well as *lactic acid* is markedly affected.

GABBE, E. (WÜRZBURG). Über die Bedeutung des Glutathions für die Oxydationen.

Bestimmt man das Glutathion (+Thionein) nach *Tunncliffe* in der Modifikation von *Perlweig* und *Delure* in den Blutkörperchen, so findet man im arteriellen Blute nur etwa 20 Procent (0 bis 42 Procent) der im venösen Blute nachweisbaren Menge. Dies deutet darauf hin, dass die SH-Verbindungen in der Lunge grösstenteils in die Disulfidform überführt werden. Die hierdurch veranlasste Sauerstoffbindung kann unter günstigen Umständen 10 Procent des gesamten Sauerstoffverbrauches betragen. Alkalisirt man das Trichloressigsäure-Filtrat des Blutes, so kann die dann eintretende Sauerstoffbindung in Barcroft-Manometren direkt gemessen werden. Dieselbe ist bei Verwendung von Blut aus dem rechten Herzen beträchtlich grösser als bei arteriellem Blute.

Bei Sättigung arteriellen Blutes mit Kohlensäure werden die Disulfide wieder hydriert; entsprechende Steigerung der Wasserstoffzahl durch andere Säuren führt nur dann zur Hydrierung, wenn zugleich ein Teil des Hämoglobins reduziert wird, z. B. durch Sättigung mit Stickstoff.

Die Gesamtmenge des Glutathions im Blute kann in wenigen Stunden um 30 bis 45 Procent zunehmen bei Verminderung des Sauerstoffpartialdruckes in der Inspirationsluft, nach akuten Blutverlusten, ferner bei Anämie durch Phenylhydrazinvergiftung. Starke Muskelarbeit steigert ebenfalls den Glutathiongehalt des Blutes um 50 bis 70 Procent; zugleich nimmt der Glutathiongehalt der willkürlichen Muskulatur um etwa 30 Procent ab (Enteiuweissung der Muskeln mit Wolfraamsäure, Bestimmung der sH-Gruppen mit Ferricyankali in stark saurer Lösung).

Nach diesen Befunden nimmt der Glutathiongehalt der Blutkörperchen regelmässig dann zu, wenn die Ansprüche an die Atmungsfunction dieser

Zellen abnorm gesteigert sind. Es verdient Beachtung, dass wir es bei der Abnahme des Glutathiongehaltes der Muskeln mit einer dem Eiweissstoffwechsel zugehörigen Substanz zu tun haben.

GAEBLER, OLIVER HENRY (DETROIT). The Determination of Creatinine in Blood.

Improvements of procedures previously used by the writer in isolating creatinine from normal and retention blood have made these procedures practically quantitative and adaptable to colorimetric determination of creatinine in 20 cc. of Folin-Wu blood filtrate. The separation of creatinine from other chromogenic substances is effected by means of adsorbing it on Lloyd's reagent and releasing it therefrom with magnesium oxide suspension.

Proving by isolation that the compound so determined is creatinine was complicated by the fact that the residue of material adsorbed by Lloyd's reagent from blood filtrate and released again contains peptone, which interferes with all quantitative precipitations of creatinine. In the case of blood from human nephritics and nephritic dogs it was found possible to isolate all of the creatinine determined. In the case of blood from normal dogs, the proportion of peptone and other substances to creatinine in the residue is such that a quantitative separation has not been accomplished, although the percentage of creatinine recovered compared favorably with recoveries from known mixtures of creatinine and peptone.

GAMBLE, J. L., P. DRINKER and L. A. SHAW (BOSTON). Demonstration of Apparatus for the Prolonged Administration of Artificial Respiration to Infants, Children and Adults. (Demonstration)

GARREY, W. E. and VIRGINIA BUTLER (NASHVILLE, TENNESSEE). Physiological Leucocytosis.

A recumbent posture for one hour and state of complete mental and physical relaxation, reduces the leucocyte count to a minimum—the basal norm. On 80 subjects the basal count was between 5,000 and 6,000, a few lower; any variation in the basal count is a certain index of disturbance of the basal state. In a given individual the basal count is constant from day to day. A basal count of 7,000 or over in normal subjects is evidence of mental or physical unrest or discomfort. The largest possible meal will not cause the slightest increase in the basal leucocyte count, a crucial disproof of the existence of digestive leucocytosis. Passive or active postural changes raise the count instantly. An activity level from 60 per cent to 100 per cent above the basal level is thus attained; this level is maintained with fluctuations (rhythms ?), the extent of which are dependent upon the variations in muscular and mental activity of the subject. The increase in the leucocyte counts is proportional to the severity of muscular exercise—in a quarter mile race lasting less than one minute the count has been raised to 35,000 per cubic millimeter. Mild grade physiological leucocytoses are due chiefly to an increase in the polymorphonuclear neutrophiles. Very high grade leucocytoses may show a preponderance of lymphocytes. In a basal individual nervous and psychic factors may induce a high grade leucocytosis. Acute cutaneous stimulation as by a dash of ether, raises the count from 5,000 to 8,000, or even 10,000. Pain may raise the leucocyte count to 20,000 in a subject resting

in bed and be mistaken to indicate infection. A mental ("psychological") test raises the basal count to an activity level and the emotive states of apprehension, fear, rage, etc., likewise produce a marked leucocytosis. The changes are attributable to circulatory shifts with the liberation of leucocytes trapped in unused capillaries.

GARRY, R. C. (GLASGOW). **Coördination between Rectum and Sphincters of the Arms.**

GASSER, H. S. and JOSEPH ERLANGER (ST. LOUIS). **The Method of Recording the Action Potential of Nerve with the Cathode Ray Oscillograph. (Demonstration)**

Apparatus will be demonstrated by which the response to a single stimulus as well as the standing wave produced by synchronized repeated stimuli may be photographically recorded.

GAUTRELET, J. (PARIS). **L'axographe, appareil permettant de tracer des ordonnées sur papier enfumé. (Démonstration)**

Nous exprimons le voeu que figurent systématiquement sur les tracés physiologiques les ordonnées indispensables à tout graphique: cette nécessité s'impose, qu'il s'agisse de mesurer ou de comparer surtout les modifications de la pression artérielle, les variations de l'amplitude cardiaque ou respiratoire, l'hyper ou l'hypotonie de l'intestin ou de l'utérus isolé, etc.

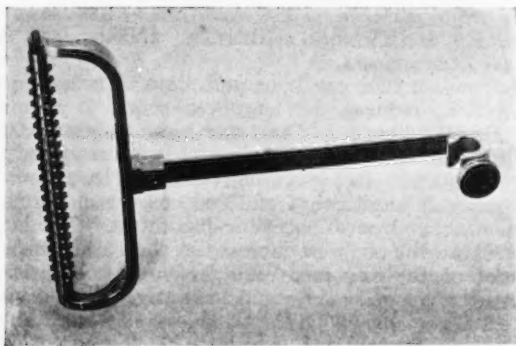


Fig. 3

L'Axographe que nous avons demandé à la maison Boulitte de construire est composé d'une série de molettes à dents régulièrement distantes, taillées sur un cylindre métallique leur servant d'axe mobile et supporté par une lame flexible en permettant l'application exacte contre le cylindre enregistreur; il permet d'obtenir sur papier enfumé le tracé de 20 lignes parallèles, discontinues, horizontales figurant d'icrètement les ordonnées à intervalles d'un demi centimètre.

GAYET, RENÉ et MAYLISS GUILLAUMIE (PARIS). **La Régulation Intra-pancréatique de L'Insulo Sécrétion.**

Chez des chiens diabétiques et chez des normaux, nous avons greffé sur les vaisseaux du cou un ou deux pancréas ou un fragment de pancréas prélevés chez un autre chien. Dans ces conditions, qui excluaient pour la première fois avec une certitude absolue toute intervention des centres nerveux, le fonctionnement insulino-sécrétoire a été non seulement évident, mais physiologiquement réglé avec une précision remarquable. La glycémie a été ramenée et maintenue à un taux physiologique, alors même que le total de tissu pancréatique greffé est deux fois supérieur ou 15 fois inférieur à la quantité que possédait le chien perfuseur avant sa depancréatation; dans le dernier cas, la chute s'est produite en un temps plus long. Sous l'influence de la greffe, le depancréaté se comporte vis-à-vis des hyperglycémies (par injections intraveineuses de glucose ou d'adrénaline) exactement comme le chien ayant son pancréas in situ. Un même pancréas implanté chez 3 chiens diabétiques, successivement, agit parallèlement sur chacun. Enfin le pancréas greffé répond directement par une réaction hypoglycémiant à l'injection directe et continue de glucose dans son artère afférente.

GERARD, R. W. (CHICAGO). **The Response of Nerve to Asphyxia and to Carbon Dioxide.**

Isolated amphibian and mammalian sciatics have been studied by means of their action potentials, their attached muscles and their oxygen consumption. For the former studies a partitioned chamber was used with six selective lead electrodes, a slow galvanometer (usually with a condenser in series) for recording, and tetanizing frequencies of 90 and 300 a second for stimulating. On passing nitrogen, carbon dioxide or carbon dioxide-oxygen mixtures through the center partition, marked changes in "total action potential" were observed at the leads from this partition and, to a lesser extent, from those above it, *i.e.*, nearer to the stimulus. These distant effects do not result from diffusion of substances along the nerve nor primarily from resistance changes in the exposed region, changes in the resting potentials, nor in flow of action currents.

When carbon dioxide (10-90 per cent) is admitted there is a rapid rise in "total action potential" to a value of 100-300 per cent above the initial one, the increase being most marked with slower tetanization. A simultaneous rise in threshold of the same magnitude occurs in the exposed region of nerve but not above it. On removing carbon dioxide with an oxygen stream, there is a further rapid rise to a peak value, and then a more gradual fall to the original level.

On replacing oxygen in the center partition by a current of pure nitrogen, there is at first often a rise in action potential lead from this partition. In one-half to one hour the values begin to fall and with increasing rapidity till no response is obtained. Of the two electrodes in the nitrogen partition the one farthest from the stimulus always fails first. The response obtained from the electrodes above the nitrogen begins to increase as the response from those in it falls. The resting potential from the nitrogen region falls (less positive) during this period. The time for asphyxiation decreases with rise in temperature and is less for nerves with a high resting O_2 consumption. On readmitting oxygen the action potentials rise very rapidly to values several hundred per cent greater than the initial ones and

then slowly fall over hours to the initial level. The distal nitrogen lead rises to a later maximum than the proximal. Both respond to slow stimulation more than to fast. The leads above the asphyxiated region show a similar behavior. Oxygen-free Ringer's solution does not affect the asphyxiation or recovery.

Methylene blue solution may modify the course of asphyxiation and increases oxygen consumption 40%. HCO_3^- also increases oxygen consumption.

Conclusions are drawn from these data on the mode and mechanism of the action of these agents on nerve.

GESELL, ROBERT, THEODORE BERNTHAL, GRACE GORHAM and HUGO KREUGER (ANN ARBOR, MICHIGAN). **Effects of Lowered Alveolar Oxygen on Various Respiratory Phenomena.**

In these experiments we have attempted to give quantitative consideration to a relatively large number of respiratory factors: tidal air, pulmonary ventilation, respiratory movements, expired oxygen, expired carbon dioxide, expiratory quotients, oxygen consumption, lactic acid content of the blood, carbon dioxide capacity of the blood, volume-flow of blood, blood pressure, hydrogen ion concentration of the blood, energy available in calories from oxidations, energy available from anaerobic processes, the relation of shortage of oxygen consumption to the accumulated lactic acid, the relation of excess oxygen consumption above normal to the removal of lactic acid, carbon dioxide expired over or under the amount required by oxidations, the relation of lactic acid metabolism to the liberation and retention of carbon dioxide, the proportion of fixed acid which combines with bicarbonate and the proportion which reacts with other buffer systems.

Constant pulmonary ventilation was administered. Expired oxygen, expired carbon dioxide, volume flow of blood and blood pH were recorded by continuous electrometric methods and checked with discontinuous methods.

On account of the large number of items and on account of their interrelation a brief analysis is difficult. These abstracts must, therefore, be considered preliminary.

Administration of gaseous mixtures low in oxygen decreased the hydrogen ion concentration and the carbon dioxide capacity of arterial blood and increased the lactic acid content and augmented carotid flow. Expired carbon dioxide was reduced but not in proportion to the reduction in oxygen consumption. The expiratory quotient was increased. Assuming for purposes of computation that lactic acid is evenly distributed between the blood and tissues it was found that oxygen shortage in cubic millimeters per kilogram over lactic acid accumulated in milligrams per kilogram was variable. The average value was 187. Computing the relationship between the lactic acid liberation and the liberation of carbon dioxide in excess of that called for by the oxygen consumption and expiratory quotient preceding administration of low oxygen an index of the effectiveness of the accumulated lactic acid in driving off combined carbon dioxide was obtained. This figure varied greatly. The average was approximately 45 per cent. The total number of calories liberated during the period of lowered alveolar oxygen by oxidation and liberation of

lactic acid was usually less than during the period of normal oxidation. In some instances it was greater. In one experiment the energy derived from the liberation of lactic acid was equal to the energy derived from oxidations. On readministration of room air these processes were reversed in varying degrees.

GESELL, ROBERT, GRACE GORHAM, HUGO KREUGER and THEODORE BERNTHAL (ANN ARBOR, MICHIGAN). **Effects of Intravenous Injection of Sodium Cyanide on Various Respiratory Phenomena.**

Intravenous injection of sodium cyanide sufficient to lower the rate of oxidations increased the hydrogen ion concentration and the lactic acid content of the blood and the flow of carotid blood and decreased the carbon dioxide combining power of the blood. Expired carbon dioxide though reduced was in excess of that required by the oxidations and the expiratory quotient. The increase in expiratory quotient was variable, apparently depending possibly on the amount of cyanide injected but on the particular animal as well. Assuming as in the preceding experiment that the lactic acid is evenly distributed between the tissues and the blood the average value of oxygen shortage in cubic millimeters per kilogram over lactic acid accumulated was found to be smaller than that obtained with lowered alveolar oxygen. This is indicative of a rapid formation of lactic acid and a liberal liberation of energy by anaerobic processes. Individual experiments show a larger ratio, the more inclusive the period following injection, suggesting possibly a slow diffusion of acid into the blood stream or a lessened effectiveness of the anaerobic processes the greater or more prolonged the injection. The effectiveness of lactic acid in liberating combined carbon dioxide appeared to be approximately equal to that found in the experiments on lowered alveolar oxygen. The total energy liberated in calories from oxidation and from anaerobic processes (liberation of lactic acid and heat formed by combining with base) was frequently increased by the administration of cyanide. These phenomena were variably reversed during recovery. Recovery from cyanide injection was on the whole not as complete as from lowered alveolar oxygen.

GESELL, ROBERT, HUGO KREUGER, THEODORE BERNTHAL and GRACE GORHAM (ANN ARBOR, MICHIGAN). **Effects of Hemorrhage on Various Respiratory Phenomena.**

Hemorrhage sufficient to appreciably lower the carotid flow of blood produced a momentary fall in hydrogen ion concentration which was followed by a sustained increase. The lactic acid content of the blood was increased and the carbon dioxide combining power was frequently decreased in corresponding degree. Oxygen consumption was decreased out of proportion to the decrease in expired carbon dioxide resulting in an increased expiratory quotient. The ratio of shortage of oxygen consumption to accumulation of lactic acid was approximately that of the lowered alveolar oxygen experiments. The effectiveness of lactic acid in liberating carbon dioxide as measured during the period of hemorrhage was low but when including the period of injection the usual figure was obtained. This is suggestive of physical retention of carbon dioxide due to impaired circulation. The markedly augmented elimination of carbon dioxide on reinjection supports this suggestion. Reinjection led to a marked overshooting of oxygen consumption and carbon dioxide elimination tempo-

rarily accompanied by a high expiratory quotient. With further recovery the expiratory quotient diminished. Not infrequently the hydrogen ion concentration of the arterial blood was temporarily increased to be followed by a recovery toward pre-hemorrhage.

GESELL, ROBERT, HUGO KREUGER, THEODORE BERNTHAL and GRACE GORHAM (ANN ARBOR, MICHIGAN). **Effects of Intravenous Injection of Sodium Bicarbonate on Respiratory Phenomena.**

Large intravenous injections of sodium bicarbonate produced profound effects on gaseous exchange and on acid metabolism. Oxygen consumption and carbon dioxide elimination in some experiments were increased from 200 to 300 per cent. The carbon dioxide elimination was in great excess of that required by rate of oxidations and magnitude of the expiratory quotient. The lactic acid content of the blood was markedly increased. Assuming that all of the lactic acid combines with bicarbonate the excess carbon dioxide eliminated above that accounted for by oxidations cannot be accounted for by the lactic acid. The effectiveness of lactic acid to combine with bicarbonate computed as in the other experiments varied from 52 per cent to about 160 per cent with an average figure of 99 per cent. Since the usual efficiency of lactic acid in liberating carbon dioxide under other conditions is approximately 40 per cent the results with bicarbonate support our earlier suggestion (Gesell and McGinty) that the increased flow of blood and increased carbon dioxide pressure of the blood produced by the addition of sodium bicarbonate to the buffer system of the blood account in part for the increased expiratory quotient. The combined energy from oxidations and formation of lactic acid may be enormously increased. In one instance it increased from 1037 calories per kgm. hour to 3777. Of this amount 855 were derived from the formation of lactic acid.

GESELL, ROBERT, HUGO KREUGER, GRACE GORHAM and THEODORE BERNTHAL (ANN ARBOR, MICHIGAN). **Effects of Intravenous Injection of Hydrochloric Acid and of Administration of Carbon Dioxide on Respiratory Phenomena.**

The administration of hydrochloric acid and of carbon dioxide produced decided changes in the hydrogen ion concentration of the blood. Recovery was more complete following administration of carbon dioxide. Hydrochloric acid always produced a definite reduction in the carbon dioxide combining power. In some instances such effects followed administration of carbon dioxide. The effectiveness of hydrochloric acid to combine with bicarbonate and liberate carbon dioxide varied. Under more normal conditions the efficiency was similar to that of lactic acid formed within the body. Following a previous administration of sodium bicarbonate the effectiveness of hydrochloric acid to liberate carbon dioxide was markedly increased. In one experiment the computed efficiency was 95 per cent. Both hydrochloric acid and carbon dioxide lowered the rate of oxidations. Despite the lowered oxidations blood lactic acid commonly diminished. This coincidence of disappearance of lactic acid and decreased oxidation seems in accord with accumulation of blood lactic acid during increased oxidation on the administration of sodium bicarbonate. Since impaired oxidation leads to increased cellular acidity and since increased cellular

acidity leads to impaired oxidations the inter-relation of these two factors must be considered in the analysis of respiratory control.

GIES, WILLIAM J. (NEW YORK). **On the Problem of Nutrition within the Enamel of Fully Formed Teeth.**

Various destructive changes that occur in the enamel of fully formed human teeth have been ascribed to abnormal nutrition *within* the enamel. A tendency erroneously to regard effects of direct chemical action by simple diffusion as evidence of "metabolism," or of "nutrition," has been noted.¹ The proof that enamel contains protein² has induced some investigators to assume that its presence indicates *intrinsic* nutritional capacity, regardless of the nature of the protein, and also despite the fact that, although permeable to water and various substances in aqueous solution, enamel completely lacks power of self-repair after injury and has no cellular nuclei. Theodor Rosebury, D. D.S., and the author have recently found that the contained protein is chiefly if not wholly keratin. That it is not associated with *intrinsic* nutritional changes in the enamel of fully formed teeth is indicated by the writer's further observation that conventional tests for tissue enzymes, applied to pulverized enamel from freshly extracted teeth, have been completely negative. Similar studies of abnormal enamel will be undertaken.

GILSON, A. S., JR., and E. IRVINE-JONES (ST. LOUIS). **Threshold Cardio-Inhibitory Effects of the Right Vagus.**

The right vagus of the turtle was dissected free from the sympathetic trunk in the neck and was stimulated. Specimens from three species of the genus *Pseudemys* were used. Maximum effects of "cardiac inhibition" were obtained with rates of six or eight stimuli per second. Slower or faster rates with nearly threshold strength of stimulation showed less effect.

Stimulation, with stimulus strengths *close to threshold* and at a rate of about eight per second, was carried out and observations were made without attachments to the heart other than a thread attached to the frenum which served to lift the ventricle. It was found that the marked effects of threshold vagal stimulation upon auricular and ventricular rates were largely due to the development of sino-auricular block. In some cases it was possible to hold the auricles and ventricle in standstill for several minutes without cessation of sinus beat. If, during a period of vagal stimulation, an impulse was conducted to such distance that the auricles responded, there *invariably* promptly followed a ventricular response. The sinus beat was rarely continued after its rate had been reduced to about half the normal, and usually before that time was reached there was standstill of the rest of the heart due to sino-auricular block. Escape from sinus inhibition occasionally occurred. This might be as uncondacted or as conducted sinus beats. Application of electrical stimuli to the auricles (either right or left) during the course of a period of inhibition showed their irritability to be either unchanged or slightly increased. *Invariably* response of the auricles to such stimuli was transmitted to the ventricle. Comparison of these results with other experiments which have

¹ Gies: Journ. Dental Res., 1926, vi, 146.

² Bödecker and Gies: Proc. Soc. Exper. Biol. and Med., 1924, xxii, 175. Also Gies: Journ. Dental Res., 1926, vi, 143.

been performed indicate a rather localized sinus innervation by the vagus fibers stimulated at these threshold strengths.

GOLDSCHMIDT, SAMUEL, assisted by AMBROSE HUNSBERGER, JR. (PHILADELPHIA). The Diffusion Rate of Ions as Affected by the Presence of Other Ions in a Solution.

The passage of chlorine ions out of a solution of sodium chloride within the large intestine is accelerated by the simultaneous presence of sodium sulphate within the solution (Goldschmidt, S. and A. B. Dayton, Amer. Journ. Physiol., 1919, xlviii, 459). This phenomenon may be the result of processes within the cells of the intestinal wall, or, conceivably, of forces which are operative within the solution itself. The present work was undertaken to investigate the effect of one ion upon the diffusion rate of another—in general, to discover some of the factors which may modify the intrinsic mobility of ions.

The rate of movement, in free diffusion, of Cl^- from an aqueous solution of a chloride to pure water has been compared with the rate of movement of the Cl^- when a salt of another anion is present. When the cation of the two salts is the same; or, if different, when the intrinsic mobility of the two cations is the same, then:

1. No detectable change in the rate of diffusion of Cl^- is produced when the added anion is univalent.
2. An increase in the rate of diffusion of Cl^- results when the added anion is divalent.
3. The diffusion rate of Cl^- is still further increased when the added anion is trivalent.

GOLLWITZER-MEIER, K. (FRANKFURT A.M.). Venensystem und Regulierung des venösen Rückflusses.

Bericht über tierexperimentelle Untersuchungen an Hunden, bei denen gleichzeitig der Venendruck in verschiedenen Venen gemessen wurde (Pfortader, Vena cava inferior und superior, Vena hepatica) neben Bestimmungen des Herzminutenvolumens (nach der Fickschen Methode) oder Aufzeichnung des Herzplethysmogramms. Die Untersuchungen wurden angestellt bei O-Mangel und bei CO_2 -Einatmung und zwar sowohl bei intakten als bei durchschnittenen Splanchnici und bei Ausschaltung der Nebennieren.

GOLLWITZER-MEIER, K. und ERNST SIMONSON. (FRANKFURT A.M.) Über die Beziehungen zwischen Sauerstoffverbrauch und Milchsäurebeseitigung nach körperlicher Arbeit.

Auf Grund der Untersuchungen von Hill, Long und Lupton hatte man allgemein die Vorstellung angenommen, dass der während und nach körperlicher Arbeit erhöhte Sauerstoffverbrauch grösstenteils durch die oxydative Beseitigung der Milchsäure bedingt sei, wobei sich auch am ganzen Menschen die Beseitigung der Milchsäure in gleicher Weise abspiele wie in den Versuchen von Meyerhof am isolierten Froschmuskel. Da uns die Versuche von Hill, Long und Lupton für die vorliegende Frage nicht vollkommen beweisend erschienen, entschlossen wir uns, die Versuche bei einer geeigneteren Standardarbeit (30 nach dem Takte eines Metronoms innerhalb 1 Minute geleistete Kniebeugen) zu wiederholen. Nach einer derartigen Arbeit verfolgten wir das Absinken des Sauerstoffverbrauches

in 150 Versuchen an 70 normalen V.P. In den meisten Fällen erreicht hier der Sauerstoffverbrauch 6-7 Minuten nach beendeter Arbeit, seltener nach 10-12 Minuten wieder das Ruheniveau. Der Milchsäurespiegel im Blut ist dagegen noch stets 22 Minuten nach beendeter Arbeit deutlich erhöht. Die Abnahme der Milchsäure, wobei wir von der wohl zulässigen Annahme ausgehen, dass 50 Procent des Körpergewichtes im Diffusionsgleichgewicht mit der Blut-Milchsäure stehen, müsste beim Bestehen der Meyerhofschen Reaktion der oxydativen Milchsäurebeseitigung am ganzen Menschen im Respirationsversuch noch messbar sein. Die Beseitigung der Milchsäure am ganzen Menschen verläuft nach unseren Versuchen ohne messbare Erhöhung des Sauerstoffverbrauchs; wir glauben uns daher zu dem Schluss berechtigt, dass die Beseitigung der Milchsäure am ganzen Menschen in einer ökonomischeren Weise erfolgt als im isolierten Froshmuskel. Andererseits wird im Anfang der Erholung mehr Sauerstoff aufgenommen, als es nach Hill bei Bestehen der Meyerhofschen Reaktion der Fall sein dürfte. Von einer Parallelität zwischen Oxydation und Milchsäurebeseitigung, d.h. von einer gesetzmässigen festen Beziehung zwischen beiden Vorgängen kann daher nicht die Rede sein.

GORINI, C. (MILAN). **Physiologic Mutation and Dissociation of the Acidoproteolytes.**

Acidoproteolytes or mixed ferments are the physiologic group of bacteria (detected by me in 1892-94¹) which attacks *simul'aneously* carbohydrates and proteins, being able to peptonize in an acid medium with a pH = 4.5 to 5.0. Since I have been a pioneer in giving to the bacteriological investigations a physiologic-biochemical address, which I think is most important for the progress of the bacteriology.

The identification of acidoproteolytes is not always easy for two reasons: 1, their sensibility towards the environmental factors, their metabolism being strictly dependent upon the conditions of life notably in regard to air, temperature and substrate; 2, their great functional heterogeneity and variability because of individual physiologic divergencies of their cells, every species, strain and colony being made up of cells with different metabolism, some prevalently saccharolytic, others prevalently proteolytic.

Hence acidoproteolytes are susceptible of very pronounced physiologic mutation and dissociation phenomena,² notably in milk.

I have described acidoproteolytes in the genus *Coccus* (*Mammococcus*,³ *Gastrococcus*, *Caseococcus*, *Enterococcus*) as well as in the genus *Bacillus* (*Bacillus acidificans presamigenes casei*⁴ belonging to *Subtilis* group). All are dissociable in S type colonies with more isolated and saccharolytic cells, and R type colonies with more long-chained and proteolytic cells.

By my method of climbing culture⁵ for isolation of motile organisms (*B. proteus*, *typhi*, *tetani*, etc.), as well as for detection of motile phases of evolution (*B. megaterium*, *mycoides*, *anthracis* etc.), motile S type is

¹ Atti Laboratori Sanità Pubblica, Ministero Interni, Roma, 1892.

Rivista Igiene e Sanità Pubblica, 1893, iv, 549.

Giornale, R. Società Ital. Igiene, 1894, xvi, No. 4, 129.

² Rend. R. Acc. Lincei, 1921, xxx, 312.

³ Rend. R. Ist. Lomb. Sci. Lett., 1901, xxxiv, 1279.

⁴ Rend. R. Acc. Lincei, 1902, xi, 159.

⁵ Rend. R. Ist. Lomb. Sci. Lett., 1904, xxxvii, 939.

⁶ Rend. R. Ist. Lomb. Sci. Lett., 1903, xxxvi, 601 and 1916, xlix, 986.

dissociable from the relatively un motile R type of the acidoproteolytic bacillus.¹

By thermobiotic culture at 50-70°C. strictly thermophilic strains are dissociable from the S type, while at most thermotolerant strains are dissociable from the R type.²

Assuming that the unstable S type corresponds to the juvenility of the microorganism, it is verisimilar that motility as well as thermophily are properties of those cells which are in a certain phase of germination, in a particular state of the protoplasm.

GOSS, HAROLD and CARL L. A. SCHMIDT (BERKELEY). **The Influence of the Reaction of the Diet upon the Calcium and Phosphorus Balances in Rats During the Period of Pregnancy and Lactation.**

Rats were placed on constant diets and periodic collections of excreta were analyzed in order to follow the calcium and phosphorus balances during the control and the period of pregnancy and lactation. All of the necessary factors were included in the diet. The reaction of the diets was varied. The reactions per 100 grams were: no. 1, 410 cc. N/10 NaOH (by addition of CaCO_3); no. 2, 280 cc. N/10 HCl (by addition of HCl); and no. 3, 440 cc. N/10 NaOH (by addition of NaHCO_3). The calcium content of all diets was approximately 750 mgm. and the phosphorus content 500 mgm. per 100 grams of food. Whenever possible each of the experiments was carried through several cycles of pregnancy and lactation.

At the onset of pregnancy and prior to parturition, animals maintained on diet no. 1 stored both calcium and phosphorus. During the lactation period the animals were in negative balance with respect to these elements. Exceptions to these statements were, however, found. The losses were usually made up during the period following lactation. There was no definite quantitative correlation between the calcium and phosphorus balances indicating that in part at least the metabolism of these elements varies independently.

When diet no. 2 was fed, results which are essentially similar to those noted in the first series of experiments were obtained. On account of failures to implant, the data are not as complete as in the experiments of the first series. When diet no. 3 was fed, the losses of calcium and phosphorus during the period of lactation appear to be greater than in any of the experiments of the previous series. It was shown, however, that the animals stored both calcium and phosphorus both during the period of pregnancy and after the period of lactation.

Experiments were also carried out on rats fed a diet deficient in vitamin E. In general, the animals stored both calcium and phosphorus during the period of pregnancy. Resorption of the fetus terminated the pregnancy. On addition of vitamin E to the diet prior to the onset of pregnancy, the usual type of calcium and phosphorus balance curves previously noted was obtained. During the periods of pregnancy, the storage of calcium and phosphorus was usually greater than the amounts estimated in the fetus at birth.

¹Rend. R. Acc. Lincei, 1927.

²Rend. R. Acc. Lincei, 1928.

GOTTSCHALK, ALFRED (STETTIN). **Der Angriffspunkt der Kohlenhydrate bei ihrer antiketogenen Wirkung.**

Auf geeignete Fett-Eiweisskost gesetzte Menschen scheiden Acetonkörper aus. Kohlenhydratzufuhr beseitigt die Ketonurie prompt. Diese alte Beobachtung hat verschiedene Deutungen erfahren. So hat die Embdenschule die antiketogene Wirkung der Kohlenhydrate lediglich auf eine Verdrängung des Fettes aus den Abbauvorgängen zurückgeführt. Nach einer anderen insbesondere von Woodyatt und Shaffer vertretenen Theorie gehen gewisse Spaltprodukte der Glucose mit Acetessigsäure bzw. β -Oxybuttersäure eine chemische Reaktion unter Bildung von leicht oxydablen Substanzen ein.

Es wurde auf folgende Weise versucht, zur Klärung dieser Frage beizutragen:

Gesunde Menschen wurden auf Fett-Eiweissdiät gesetzt und die unter diesen Bedingungen ausgeschiedenen Acetonkörper 6 Tage lang quantitativ bestimmt. Am 7. und 8. Tage erhielt die Versuchsperson zu obiger Kost 30 g buttersaures Natrium zugelegt. Am 9. Tage wurden zur Standarddiät 30 g buttersaures Natrium + 150 g Kohlenhydrate verabfolgt. Der Versuch ergab einen beträchtlichen Anstieg der Ketonurie unter dem Einflusse der Buttersäurezufuhr. Bei gleichzeitiger Darreichung von Buttersäure und Kohlenhydraten war der Urin frei von Acetonkörpern. Es kann demnach die bei geeigneter Diät durch reichliche Zufuhr von Buttersäure hervorrufbare Ketonurie erheblichen Grades durch Kohlenhydratgabe beseitigt werden. Hierdurch ist erwiesen, dass bei obiger Versuchsanordnung der Angriffspunkt der Kohlenhydrate bei ihrer antiketogenen Wirkung auf der Buttersäurestufe erfolgt.

Bezüglich des Chemismus dieses Eingreifens der Kohlenhydrate in den Fettsäurestoffwechsel darf auf Grund zahlreicher Beobachtungen betr. häufiges Auftreten von Ketonurie bei normalem bzw. nahezu normalem Zuckerumsatz (Kinder, Schwangere) sowie im Hinblick auf die nur geringfügige provozierbare Ketonurie bei gewohnheitsmässig lediglich von Fleisch und Fett lebenden Organismen (Eskimo, Hund) daran gezweifelt werden, dass zwischen Kohlenhydratspaltprodukten und Buttersäurederivaten eine in konstanten Mengenverhältnissen sich vollziehende Reaktion statthat. Vielmehr wird angenommen, dass in energetischer Kuppelung mit gleichzeitig stattfindenden Oxydationsprozessen ein Teil der anfallenden Buttersäure bzw. β -Oxybuttersäure zu höheren Fettsäuren resynthetisiert wird. Dafür sprechen neuere Versuche betr. die anti ketogene Wirkung von 1-l-Verbindungen (Methyl-alkohol, Formaldehyd, Ameisensäure).

GRAFE, E. und R. E. MARK (WÜRZBURG). **Paradoxe Stoffwechselwirkungen nach Milzfütterung.**

Unsere Kenntnisse über die spezifisch-dynamische Wirkung der Eiweisskörper sind fast ausschliesslich aufgebaut auf Untersuchungen des Fleisches bzw. der in ihm enthaltenen Aminosäuren. Dabei wurde stillschweigend die Voraussetzung gemacht, dass zwischen den einzelnen Organen des Organismus kein nennenswerter Unterschied besteht. Schon eigene Untersuchungen über die Leber haben ergeben, dass Fütterung dieses Organs einen weit geringeren, manchmal sogar völlig fehlenden spezifisch-dynamischen Einfluss auf die Oxydationen ausübt. Erst recht abweichend vom

Fleisch verhält sich die Milz, vor allen Dingen dann, wenn sie häufiger gereicht wird. Während bei der ersten Fütterung hin und wieder eine annähernd normale, manchmal auch eine herabgesetzte spezifisch-dynamische Wirkung eintritt, kann sie in anderen Fällen von vornherein fehlen oder in ihr Gegenteil sich umkehren, d.h. es kommt in der Regel zu einem mehr oder weniger starken Absinken der Verbrennungen, das über viele Stunden anhält, sodass die Werte des folgenden Morgens noch subnormal liegen. In gleicher Weise wie beim Normalen gelingt es auch bei pathologischen Stoffwechselsteigerungen, vor allen Dingen bei Basedowkranken, Erniedrigung zu erzielen und so unter Umständen den erheblich gesteigerten Stoffwechsel durch langdauernde Milzdarreichung auf normale Werte herabzusetzen. Im weiteren Gegensatz zum Fleisch wirkt Milzfütterung nicht steigend, sondern eher erniedrigend auf den Blutzucker, ferner beim Diabetiker nicht acidosesteigernd, sondern eher antiketogen. Über die Ursache dieses eigentümlichen Verhaltens des Milzgewebes lassen sich vorläufig nur Vermutungen äussern.

GREEN, ARDA ALDEN and EDWIN J. COHN (BOSTON). **Physicochemical Methods of Characterizing Proteins. IX. The Activity Coefficients of Carboxyhemoglobin in Various Salt Solutions.**

The activity coefficient of a slightly soluble substance is defined by the ratio of its solubility in a given salt solution to its solubility in the absence of salt. The solubilities, and therefore the activity coefficients, of crystalline carboxyhemoglobin have been measured in solutions of NaCl, Na₂SO₄, Na₂C₆H₅O₇, KCl, KH₂PO₄ + K₂HPO₄, (NH₄)₂SO₄, and MgSO₄.

In sufficiently concentrated solutions of sulphates and phosphates, we have previously shown that protein solubility is inversely proportional to the molecular concentration or the ionic strength, and have associated the proportionality constant with the salting out constant in the Debye-Huckel equation.

This method, although adequate for characterization, ignores the solvent action of neutral salts upon globulins, defined in Debye's equation in terms of the valence type of the saturating salt, κ a universal constant, and b the mean effective diameter of the ions in solution. The apparent valence type previously ascribed to oxyhemoglobin obtains also for carboxyhemoglobin. We may therefore write:

$$-\log \gamma = \log S/S_0 = 2 \sqrt{\mu}/(1 + \kappa b) - K_S \mu$$

S and S_0 have been experimentally determined. For carboxyhemoglobin S_0 is 20 grams per liter at pH 6.6 and 25°C. Since b is a constant whose value, as a first approximation, may be derived from the literature, only K_S remains unknown. The following values of K_S have been calculated for uni-univalent salts for which values of b are at present available.

SALT	$0.33 \times 10^6 b$	K_S
NaCl	0.775	0.09
KCl	0.816	0.15

These values of S_0 , b and K_S completely define solubility in these solutions, and yield a theoretical description of such influences of specific ions upon proteins as have been observed by Hofmeister and subsequent investigators.

GREENE, CARL H. and MARSCHELLE H. POWER (ROCHESTER, MINNESOTA). **Studies of the Blood by In-Vivo Dialysis with an Additional Note on the Comparison of the Electrolyte Equilibrium with that in Cerebrospinal Fluid and the Ultrafiltrate of Serum.**

The condition of the diffusible substances in the blood has been studied by means of the vividiffusion technic of Abel and Rowntree. Normal dogs were operated on under local anesthesia or under narcosis induced by iso-amyl ethyl barbituric acid. Heparin was used as an anticoagulant. Dialysis was carried out, in duplicate, against a hypertonic and against a hypotonic saline solution; 200 mgm. of glucose for each 100 c.c. was added to one solution but not to the other. The dialysates were examined at short intervals and the experiment was continued until complete equilibrium was reached. Analyses were then made of the blood serum, of the two dialysates, and of the cerebrospinal fluid. It is believed that this in vivo dialysis against the circulating blood gives a more satisfactory control of variable factors, such as temperature, carbon dioxide tension, hydrogen-ion concentration, and so forth, than the usual methods of compensation dialysis in vitro.

The optical rotatory power of the dialysates was determined in tubes 4 dm. in length, by means of a Schmidt and Haensch polariscope reading to 0.01 degree, with the green mercury line as a source of light. The reducing power of the blood plasma and of the dialysates was determined by both the Folin-Wu and Shaffer-Hartman (Somogyi modification) methods. Fermentation with yeast was used as an index to the amount of glucose present. Sugar equilibrium was established at or near the level in the plasma in each dialysate. Because of the effect of the nonfermentable fraction, the Shaffer-Hartman method gives higher reducing values in whole blood than does the Folin-Wu method. The sugar in the dialysates was completely fermentable, however, and in these solutions the two methods gave identical values. The rotatory values of the dialysates as obtained at the end of an experiment in which the pH of the material was 7.8 to 8.0 were lower than the reducing values, but after acidification to pH 2.0 to 3.0 the rotatory values calculated as glucose agreed with the reducing values within the experimental error.

The nitrogenous constituents of the blood, urea, creatinine, amino-acid nitrogen and the total nonprotein nitrogen, came to an equilibrium at or near the plasma level in the plasma. However, the Benedict method for the determination of uric acid uniformly gave negative results when applied to the dialysates.

A study of the electrolyte equilibrium was made, based on a comparison between the composition of the serum, calculated both in terms of the serum and of the serum-water, and of the in vivo dialysate, the cerebrospinal fluid and the ultrafiltrate of the serum. The concentrations of sodium and of potassium were slightly but definitely lower in the dialysate than in the plasma. It is generally recognized that a portion of the calcium in the serum is combined with protein. Correspondingly the concentration of calcium in the in vivo dialysate was from 60 to 70 per cent of that in the serum. The spinal fluid and ultrafiltrate contained slightly less calcium than the in vivo dialysate. The concentrations of chloride and of bicarbonate in the dialysate were higher than those in the serum but less than those in the spinal fluid. The composition of the dialysate diverges considerably from that required by a simple Donnan equilibrium and suggests

that under the conditions of these experiments the latter plays a relatively minor rôle. The effect of the volume occupied by the protein and the binding of cations by the latter in a possibly nonionizable form, likewise may have a rôle in determining the composition of the dialysate. These latter factors must likewise be considered in the study of the equilibrium between the serum and edema fluid or between the serum and the cerebrospinal fluid.

GREENE, CHARLES W. (COLUMBIA, Mo.). **The Reflex Nervous Regulation of the Coronary Circulation.**

The coronary blood vessels are supplied with vaso-constrictors by way of the vagi (Porter, 1896), and with vaso-dilators by way of the thoracic sympathetics and the stellate ganglia (Maas, 1899). These facts have been abundantly confirmed in the present investigations. The coronary vaso-constrictors are only weakly developed but the vaso-dilators are strongly developed. The mechanisms of reflex control have been sought in the present experiments.

The methods used measured the rate of flow from the coronary sinus of the dog by means of a Morawitz cannula and flow manometer. Carotid blood pressures and heart rates were recorded. The arterial pressure was equalized by an overflow reservoir attached to the femoral. The venous blood was returned through the jugular under constant pressure. Anesthesia was by ether, ether and morphine, or by hypnotics.

Well recognized afferent paths for general vascular reflexes of the trunk and viscera were explored for evidence of coronary response both before and after atropine. Coronary vasomotor reflexes were demonstrated from a wide variety of sources,—1, from stimulation of the central end of the sciatic; 2, the hepatic; 3, the coeliac ganglion; 4, the splanchnics; 5, the gastric vagus, and 6, the cervical vagus. Reflex coronary constrictions are usually mild, but dilatations are more profound. The coronary reflexes from abdominal nerves are not predictable, since they may be dilator, or constrictor, or diphasic. Vagal vaso-constrictor tone described by von Anrep was not found, but pronounced vaso-dilator tone was demonstrated especially in young animals. Efferent coronary vaso-dilator reactions have been observed through thoracic sympathetic branches as low as the sixth dorsal (left) in the dog. These observations lend support to the anoxemial theory of the origin of anginal attacks of the neural type.

GREINER, I. und J. MOSONYI (BUDAPEST). **Einfluss der Vitamine auf die chemische Zusammensetzung der Frauenmilch.**

Bei 18 stillenden Frauen wurde der Einfluss einer vitaminreichen Nahrung auf die chemische Zusammensetzung der Milch untersucht. Es wurde der Stickstoff-, Fett-, Zucker- und Trockensubstanzgehalt, die Asche bestimmt. In jedem Falle wurden zuerst innerhalb 10 Tagen, bei normaler Kost, drei Untersuchungen ausgeführt. Nachher bekam die Versuchsperson 6 Wochen hindurch täglich 40 gr. Ovaltine Dr. Wander. (vitaminhaltiges Nahrungspräparat). Nun folgten noch drei Milchuntersuchungen, die zweiwöchentlich stattfanden. Unterschiede zeigten sich bloss im Fettgehalte. In 42,1 Prozent der Fälle konnte festgestellt werden, dass der Fettgehalt der Muttermilch nach Verabreichung des vitaminhaltigen Präparates den normalen Wert beträchtlich überstieg.

In 31,6 Prozent blieb der Fettgehalt normal und in 31,6 Prozent fiel derselbe, trotz der gesteigerten Vitamineinfuhr, unter die Norm. (Der Normalwert beträgt im Durchschnitt 3,6 Prozent.) Im Stickstoff-, Kohlehydrat- und Aschengehalt zeigten sich keine Unterschiede. Der Gehalt an Trockensubstanz änderte sich mit dem Fettgehalte.—Mit den chemischen Milchuntersuchungen parallel beobachteten wir auch das Körpergewicht der Säuglinge. Im Vergleich zu den Säuglingen der bei normaler Kost (ohne Vitaminplus) lebenden Mütter, konnte in unseren Versuchen eine Gewichtszunahme von 15 Prozent festgestellt werden.

GREISHEIMER, ESTHER M. and OLGA H. JOHNSON (MINNEAPOLIS).
Glycogen Formation in Rats.

Each litter is separated from the mother on the twenty-second day, and one rat placed on each of the diets. In addition to having as much of the special diet as it can eat, each rat receives yeast, cod-liver oil and wheat germ daily. The rats are kept on the special diets for three weeks, being weighed three times each week. At the end of the period, the rats being now six weeks old, the liver and muscle glycogen contents are determined.

The following diets have been used in this study, the figure in parenthesis indicating the percentage of total calories derived from each foodstuff.

	CASEIN	CORNSTARCH	SUCROSE	LARD	SALT (185)
Diet 1.....	30 (30)	60 (59)		5 (11)	5
Diet 2.....	30 (30)		60 (59)	5 (11)	5
Diet 3.....	30 (21)		25 (17)	40 (62)	5
Diet 4.....	60 (56)		25 (23)	10 (21)	5
(Control) Diet 5.....	30 (25)		45 (37½)	20 (37½)	5

On the day on which the rats are to be killed, the feed boxes are removed at 7:30 a.m., and the animals killed two hours later. A sharp blow on the head followed by section of the cord is the method used. The liver is removed entire, placed between weighed watch glasses, and weighed to the nearest milligram. It is then placed in an equal amount of hot 60 per cent potassium hydroxide, in a boiling water bath. A space of about two minutes elapses between the blow on the head and the submersion in the alkali. The liver is completely dissolved within five minutes. The thigh muscles are removed, and treated similarly.

After digestion, aliquot portions are taken for the analyses, which are made in duplicate. We are indebted to Prof. C. Lovatt Evans of University College for valuable modification in the method, which we have used with his permission. After precipitation and hydrolysis, the sugar is determined by the Shaffer-Hartmann method.

The results are presented below.

	DIET 1	DIET 2	DIET 3	DIET 4	DIET 5 (CONTROL)
Average per cent of glycogen in liver..	3.94	4.56	4.13	2.42	3.01
Average per cent of glycogen in thigh muscles.....	0.35	0.31	0.33	0.31	0.31
Liver as per cent of total body weight..	4.74	5.43	4.79	5.20	5.17

The diets are all edible and allow growth. A representative from each litter is placed on each diet. Enough litters are being studied to permit statistical treatment of the results at a later time.

GRIFFITH, WENDELL H. and C. E. GRAHAM (ST. LOUIS). **The Effect of Liver and of Yeast on the Consumption and the Utilization of Food.**

Whole dried yeast, which is a richer source of vitamin B_1 than of vitamin B_2 , has been found to be directly related to the utilization of ingested food rather than to the consumption of food. An aqueous extract of liver, which is a richer source of B_2 than of B_1 (unpublished experiments), has been found to stimulate the appetite and to increase the consumption of food but not to affect the utilization of food.

Young male white rats were used and were kept in individual raised cages during a forty day experimental period. Rats fed a basal diet plus 150 mgm. of yeast daily grew less rapidly than controls on the stock diet. When the supplement of yeast was increased to 300 mgm. daily the rate of growth equaled that of the controls. The addition of the extra yeast increased the rate of growth 47 per cent and the food consumption only 9 per cent. When the basal diet was supplemented daily with 300 mgm. of yeast and 0.5 cc. of an aqueous extract of liver the rate of growth far exceeded that of the control animals. The added liver extract increased the rate of growth 37 per cent and the food consumption 21 per cent.

In the second series of experiments rats were fed restricted amounts of the basal diet so that equivalent quantities of food of the same calorific value were ingested daily. In these experiments the calories required per gram increase in weight during the forty day experimental period were as follows: basal diet plus 150 mgm. of yeast, 15.7; basal diet plus 300 mgm. of yeast, 12.2; basal diet plus 300 mgm. of yeast plus liver extract, 13.3. This series of experiments illustrated the effect of the yeast in increasing the efficiency of utilization of food and demonstrated that the liver extract was ineffective in this respect. Further experiments showed that this extraordinary effect on the appetite of the ingestion of liver was most marked in the first 20 day period and was hardly apparent in the second 20 day period.

GRIJNS, G. (WAGENINGEN). **Diet and Reproduction.**

On a diet of cornmeal, peanut- or cocoa-meal, hydrogenated arachis oil and a salt mixture (CaCO_3 , NaCl , KH_2PO_4 , FeSO_4) young rats grow excellently and when mated have normal litters and rear a normal percentage of the young. The second generation grows as well, but save for a single exception all males are sterile and show more or less degenerated testes. The females reproduce normally with males on stock diet.

On a diet of blood albumen, casein, hydrogenated oil, rice starch, marmite, decitrated lemon juice, McCollum's salt mixture and ostelin (a cod liver oil product from the Glaxo Co., London) nearly all females are sterile, the males on the contrary appear fertile with stock-fed females.

On a ration of blood albumen, casein, hydrogenated oil, rice starch, marmite, decitrated lemon juice, McCollum's salt mixture and an extract of carrots fertility was almost normal but none of the females could rear its young.

On a ration of whole wheat meal 250, wheat starch 125, hydrogenated fat 60, butterfat 15, casein 25, lemon juice 20, salt mixture as in corn food the percentage of young weaned was 45 per cent in the first and 25 per cent in the second generation. Addition of 2 to 4 per cent of serum albumen raised this to normal. Extraction of the albumen with ether did not decrease its effect. We found the ash of the albumen and the ether extract to have no effect.

From these facts we ought to postulate at least 3 factors controlling reproduction: one for spermatogenesis, one for the normal gestation of the female and one for lactation.

There are some indications that the latter may depend on the composition of the proteins in the ration.

GROLLMAN, ARTHUR (BALTIMORE). **Physiological Variations of the Cardiac Output of Man.**

Despite the great amount of work which has been done in recent years on the determination of the cardiac output of man, our knowledge of the physiological variations of the cardiac output under different conditions is still fragmentary. This state of affairs is the result of the great errors and difficulties involved in such determinations. The importance of the problem to the proper understanding of the physiology of the circulation rendered it essential to institute a systematic investigation of the cardiac output of man by methods which, in so far as can be tested, are of a high degree of accuracy. Such methods have been previously described by Marshall and the author (1928) and the author (1929).

In order to determine the variations of the cardiac output, a series of determinations were made on two individuals over a period of a year. The results were found to be extremely constant and reproducible from day to day, when certain precautions were taken in their determination.

Contrary to the commonly accepted view, it has been found that there exists in man a compensatory mechanism which maintains a relatively constant cardiac output despite postural changes.

The ingestion of large amounts of fluids causes a moderate rise in the cardiac output which is greater after the ingestion of isotonic saline than after the ingestion of water. The splanchnic dilatation which follows the ingestion of food is accompanied by a large increase in the cardiac output which, after a rapid rise, remains rather constant for several hours.

Psychic disturbances were found to cause an elevation in the cardiac output.

Determinations on a series of normal subjects in the truly basal condition showed the cardiac output to be a function of the surface area of the individual and to correspond to a constant arterio-venous oxygen difference.

The effects of the catamenial cycle, external temperature, physical exercise and other physiological factors on the cardiac output were also studied.

A preliminary account was also given of the results of an Expedition to Pikes Peak showing the changes in cardiac output at low barometric pressures and their relations to the processes of acclimatization.

The results demonstrate an independence of the pulse rate and cardiac output. Changes in the latter function are dependent rather on peripheral adjustments whose occurrence is essential for and concomitant with these changes in cardiac output.

GRUBER, CHARLES M. (ST. LOUIS). **The Blood Flow in Skeletal Muscles in Unanesthetized Cats as Influenced by Epinephrin.**

Hoskins, Gunning and Berry, Hartman and McPhedran, Gruber, Hartman and Fraser and Dale and Richards demonstrated that "adrenin" produces vaso-dilatation of the skeletal muscle vessels and vaso-constriction of the vessels of the skin and other tissues. Gunning and Erlanger and Gasser using large doses of adrenalin noted vaso-constriction only.

Publications of Macdonald and Schlapp, Vincent and Curtis, and Dragstedt indicate some difference in action of epinephrin on the blood pressure in anesthetized and unanesthetized animals. With these findings Gruber does not agree fully.

If epinephrin always causes a rise in blood pressure irrespective of dose in unanesthetized animals as some investigators claim one would anticipate only vaso-constriction of the vascular system.

In this work large cats were used. Under ether anesthesia both femoral arteries and veins were isolated ready for cannulation and the spinal cord cut in the lower thoracic region. Four to eighteen hours after recovery from the anesthetic the animal was used for experimentation. The blood vessels were cannulated and heparin injected intravenously to prevent clotting. All the veins, except those coming from an individual muscle or group of muscles, to one femoral vein were tied off. The blood pressure was recorded with a mercury manometer and the blood flow from the muscle in drops.

Adrenalin chloride 0.1 to 0.5 cc. of a 1:100,000 solution injected intravenously caused either a fall, no change or a rise in blood pressure at the same time it caused an increase in the rate of blood flow from the skeletal muscle. In one animal in which epinephrin caused no increase in blood pressure the rate of blood flow increased from 42 to 72 drops per minute returning to the control level soon after the injection.

Large doses of adrenalin 0.5 to 1 cc. of a 1:10,000 solution caused a rise in blood pressure, in some cases followed by a fall. During the height of increased blood pressure a decrease in rate of blood flow from the muscle was recorded. In most cases preceding and following this decreased flow an increase in blood flow was observed. This increase was recorded even though the blood pressure fell below the control blood pressure level following the rise, *e.g.*, in one cat 1 cc. of a 1:10,000 solution of epinephrin was rapidly injected intravenously and the arterial blood pressure increased from 133 to 250 mm. of mercury with a concomitant decrease in the rate of blood flow from the muscle from 38 to 13 drops per minute. Instead of the blood pressure falling to the normal level it dropped to 88 mm. of mercury, a fall of 45 mm. of mercury. Four minutes were required for the normal level to be reached and maintained. Simultaneously with the sudden decrease in blood pressure the rate of blood flow from the muscle examined increased to 88 drops per minute or four times the normal rate when the blood pressure was 146 mm. of mercury.

From these results we infer that there is no difference in the vaso-motor action of epinephrin on muscle vessels in unanesthetized and anesthetized cats. Since epinephrin produces a dilatation of the blood vessels in one region of the body and at the same time causes vaso-constriction in other regions, the blood pressure recorded must be that of the stronger effect minus the weaker.

GRÜNDBAUM, A. A. (AMSTERDAM). **Die Zeigehaltung der Hand als primitiver und pathologischer Reflex.**

In einigen Fällen mit Störungen des extrapyramidalen Systems kann man eine zwangsmässige Haltung der Hand wahrnehmen, die wie ein willkürliches Hinwerfen auf einen Gegenstand aussieht. Es ist mir gelungen dieselbe Haltung der Hand als einen Reflex zu provozieren in Fällen wo die entsprechende Kontraktur oder athesotische Bewegung nicht besteht.

Wird der Zeigefinger der lose gehaltenen Hand gezogen, überstreckt oder in vertikaler Richtung gedreht, so werden die anderen Finger entsprechend der Zeigehaltung reflektorisch gebeugt. Dass es sich um einen Reflex handelt beweist die Möglichkeit der kontralateralen Provozierung; ausserdem ist der provozierende Reiz spezifisch: Weder Schmerz und starke kalorische Reize, noch faradische und galvanische Reize rufen die Haltung hervor. Provozierbar ist der Reflex *nur* vom Zeigefinger aus. Die Reaktionszeit $\pm 0,25$ sec. entspricht der Reaktionszeit anderer Gelenkreize und weist auf cerebrale Abhängigkeit des entsprechenden physiologischen Mechanismus. Dieser Reflex, der bei diffusen Störungen des extrapyramidalen Systems kombiniert mit schwacher pyramidreichen beobachtet wird, ist bei *normalen* Kindern von zwei bis fünf Jahren fast ausnahmslos wahrzunehmen, wobei bei jungen Kindern die Provokierung nicht allein auf den Zeigefinger beschränkt ist, später aber sich bloss auf diesen Reizort konzentriert.

Es ist bemerkenswert dass die Zeit des Auftretens des Zeigereflexes zusammenfällt mit Aufhören des Wabiusski'sche Zehenreflexes (Vollzogene Reife des Pyramidensystems), dem Aufhören des Greifreflexes und mit der Zeit des normalen Auftretens des positiven Grundgelenkphänomenes von Meyer und des Reflexes von Leri. Allen Handreflexen entspricht somit wahrscheinlich derselbe allgemeine Mechanismus der in besonderen Fällen unter verschiedenen Regulierungsbedingungen entsteht. Die expressive Haltung der Hand beim Zeigen beruht ebenso auf demselben systematischen Zusammenhang des entsprechenden muskularen Mechanismen wie der Reflex und wie die analogen Kontrakturen. Die Zeigehaltung entsteht auch aus dem Greifmechanismus und ist quasi das Resultat des Greifenwollens und des Nichtgreifenkönnens.

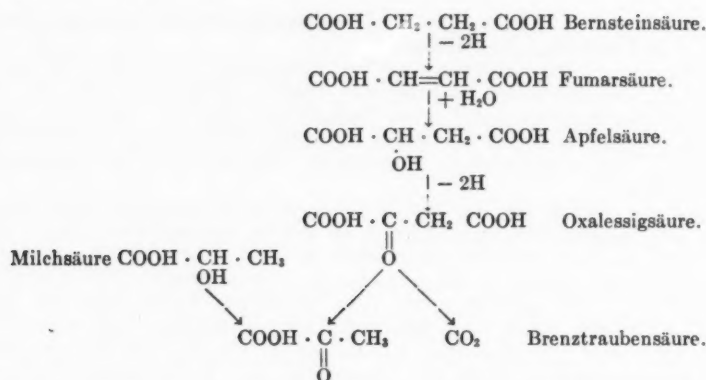
HAHN, AMANDUS (MÜNCHEN). **Über Dehydrierungsvorgänge im Muskel.**

Durch Isolierung der entstehenden Stoffe konnte gezeigt werden, dass *Bernsteinsäure*, die mit Muskelbrei und Methylenblau im Vakuum einige Stunden bei 38° gehalten wurde, durch Dehydrierung (im Sinne der Wieland'schen Theorie) in *Fumarsäure* übergeht. Letztere lagert fermentativ Wasser an die Doppelbindung an und geht dabei in *Äpfelsäure* über.

In bestimmter Weise hergestellte Muskelpräparate, die Äpfelsäuredehydrase enthalten, verwandeln die Äpfelsäure in *Oxalessigsäure*, deren Entstehung durch Abfangen mit Semikarbazid nachgewiesen werden konnte.

Eine Milchsäuredehydrase des Muskels führt Milchsäure in *Brenztraubensäure* über; auch dieser Stoff wurde durch Semikarbazid abgefangen.

Somit ist der folgende Gang der Dehydrierung im Muskel durch Isolierung aller Stoffe nachgewiesen worden:



Auch ohne Zusatz von Akzeptoren, sowie Methylenblau, findet im Muskel Dehydrierung zugesetzter Stoffe statt, wohl durch im Muskel vorhandene natürliche Akzeptoren.

HALPERT, BÉLA and MILTON THEO. HANKE (CHICAGO). The Excretion, by the Liver, and Accumulation in the Gall Bladder of Certain Organic Compounds, Particularly Dyes.

Quantitative methods were developed for estimating salicylic acid, di-iodosalicylic acid, methylene blue, eosine, erythrosine, rose bengal and tetra-iodo-phenolphthalein in bile. Salicylic acid and di-iodosalicylic acid are not excreted into the bile. Eosine, erythrosine and rose bengal are largely excreted into the bile; but they do not accumulate in the gall bladder because they are absorbed by the gall bladder mucosa about as readily as are the normal bile constituents. Only a small portion of the administered methylene blue appears in the bile. Tetra-iodo-phenolphthalein, or at least some compound containing iodine, is largely excreted in the bile. Methylene blue and tetra-iodo-phenolphthalein accumulate in the gall bladder. The experiments were conducted on rabbits and the chemicals injected intravenously in doses of 2 cc. per kilogram body weight of a 1 per cent solution.

HAMILTON, W. F., J. W. MOORE, J. M. KINSMAN and R. F. SPURLING (LOUISVILLE). Studies on the Circulation.

Determinations have been made of 1, the cardiac output; 2, the total circulation time, and 3, the mean circulation time from vein to artery. From these data one can calculate 4, the size of the intrathoracic vascular bed.

The effect of heart rate changes, hemorrhage and anemia upon these (four) factors has been studied in dogs. In man the same factors have been followed in their changes due to posture, heart rate, thyroid disturbance and cardiovascular disease.

HAMMETT, FREDERICK S. (PHILADELPHIA). A Chemical Stimulus Essential for Growth by Increase in Cell Number.

The Pb-deposit found concentrated in the meristematic region of roots of seedlings grown in Pb-containing culture solutions having been identi-

fied as a combination of the metal with sulfhydryl, and the fact having been found that mitosis is inhibited by Pb-ion while growth in cell size is not retarded, the hypothesis was developed that growth by increase in cell number is importantly factored by sulfhydryl.

I first tested this by determining the influence of extracts of the meristem region on root growth in length controlled by like extracts of the immediate distal portion of the root. It was found that stimulation was produced. Since sulfhydryl is found concentrated in the region of active mitosis of roots, the finding is consistent with the hypothesis. Further tests were made with a number of synthetic and natural -SH containing compounds, controlled by the same substances minus sulfur. It was found that stimulation of mitosis in root-tips and of reproduction of *Paramecium* consistently occurred. The conclusion from this and correlated data is that sulfhydryl is the essential stimulus to growth by increase in cell number.

HANDOVSKY, HANS (GÖTTINGEN). Über ein besonderes Verhalten der arbeitenden Skelettmuskeln männlicher Kastraten.

Der musc. tibialis ant. narkotisierter Kaninchen (3 g Urethan pro kg) wird durch elektrische Reizung des peripheren Stumpfes des nerv. ischiadicus arbeiten gelassen. Reizung mit Einzelschlägen, 170 Reize in der Minute. Normale Tiere beiderlei Geschlechtes zeigen die übliche Ermüdungskurve allmählich kleiner werdender Zuckungen. Die Muskeln kastrierter Männchen, besonders einige Zeit nach der Operation, verhalten sich völlig anders; bei ihnen treten bei maximaler Reizung zunächst Zuckungen von ungefähr der gleichen Höhe wie bei den normalen Tieren auf. Wenn aber der Höhepunkt der Bowditch'schen Treppe erreicht ist, nimmt die Leistungsfähigkeit sofort ab; sie erreicht nach 1 Minute 60% und nach 2 Minuten meist 30% der ursprünglichen Leistungsfähigkeit; in diesem Ausmaß bleibt dann der Muskel sehr lange leistungsfähig. Mit der Methode von Marey liess sich nachweisen, dass während dieses Abfalls der Leistungsfähigkeit eine Dilatation der Muskelgefäße auftritt; der Muskel erhält also genügend Sauerstoff, kann diesen nur nicht entsprechend verwerten. Da der Milchsäuregehalt von Skelettmuskeln kastrierter Männchen 2-3 mal so groß ist wie der normaler Tiere, wird angenommen, daß der Muskel der männlichen Kastraten die Fähigkeit verloren hat, Milchsäure entsprechend zu verwerten.

HANKE, MARTIN E. (CHICAGO). Further Work on the Organic Chlorides of Tissues.

Two years ago¹ we reported that the chlorides of tissues can be divided by methods of extraction with organic solvents into two fractions, either soluble or organic chloride, and ether insoluble or inorganic chloride. The organic chloride occurs in characteristic amounts in all tissues studied and composes about 50% of the total chloride of the gastric fundus mucosa and kidney, about 35% of that of the liver, pylorus, intestinal mucosa, and pancreas, while only 2 to 8% of that of blood, muscle, skin and brain. If such chlorides are esters, with chlorine attached to carbon, one might expect that their hydrolysis should involve the formation of hydrochloric acid and a neutral alcohol, $RCl + HOH \rightarrow HCl + ROH$, while their synthesis from inorganic chloride should involve the liberation of base, NaCl

¹ Hanke and Donovan: Journ. Biol. Chem., 1927, lxxiv, p. xxiv.

+ ROH \rightarrow RCl + NaOH. We have postulated therefore that these ether soluble chlorides of tissues might be concerned with the neutrality regulation of the organism and also with the local production of acid and base, e.g., the HCl of the gastric juice, and the Na₂CO₃ in the intestinal juices. Further work on these chlorides may be summarized as follows.

1. A study was made of the distribution of organic and inorganic chloride in tissues of animals in experimental acidosis and alkalosis. Acid injection doubles the total chloride of the fundus mucosa leaving the organic chloride slightly less than normal; it reduces the organic chloride of the liver almost to zero, with no change in the total chloride; it raises the organic chloride of the kidney and intestine, with a corresponding increase in the total chloride. Alkali injection leaves the total chloride of fundus mucosa and liver unchanged, with a slight decrease in organic chloride; in the kidney and intestine the total chlorides are unchanged with a slight increase in the organic chloride. The chlorides of other tissues are not changed by acid or alkali injection.

The results of acid injection although consistent for any one tissue, are not the same for all tissues; and the same can be said of the results of alkali injection. Moreover, the effects of acidosis are in no sense the opposite of those of alkalosis. Whatever the interpretation of these results, they do indicate that the hydrolysis and synthesis of ether soluble chloride is not directly related with acid or alkali formation or with neutrality regulation in tissues.

2. Studies on the chemical nature of the ether soluble chloride have shown that in aqueous solution the chloride is all completely precipitated by silver ion at once in the cold. This indicates that it is a salt, although it might be as readily hydrolysable ester. In an aqueous solution of such an ester, $\text{RCl} + \text{HOH} \rightleftharpoons \text{HCl} + \text{ROH}$ we should expect that decreasing the chloride ion activity should increase the hydrogen ion activity and vice versa. No significant effects on the pH of solutions have been observed, by varying the chloride ion activities. (We have observed that the addition of neutral silver nitrate to an aqueous solution of ether soluble tissue chloride, causes a marked fall in pH, with liberation of nitric acid. This, however, is not related to the chlorides present, and is due to the precipitation of the silver salt of a very weak fatty acid, less soluble than silver chloride, having a pK' of 7.4).

3. Analyses for sodium and potassium were made in the ether soluble chlorides of tissues, and these were correlated with the chloride equivalents.

It was found that the ratio of $\frac{\text{K} + \text{Na}}{\text{Cl}}$ is between 1.2 and 2.2. In other words, the chloride content is more than accounted for in terms of equivalents of sodium and potassium. The excess alkali metal here is probably bound by fatty acid.

These results indicate that the ether soluble chlorides of tissues are salts and *not* esters and that they are *not* associated particularly with neutrality regulation or acid or base production in the animal organism.

HANKE, MILTON THEO. (CHICAGO). **The Relation of Diet to Dental Disorders.**

Blood examinations for Ca and P and a dietary analysis have been completed on 200 cases afflicted with every type of dental disorder. The ages

ranged from 4 to 60 years. The diets were, usually, not markedly deficient in vitamin D. Some 40 per cent of the diets were markedly deficient *only in vitamin C*. It is possible, by means of a diet containing an abundance of vitamin C, to produce solid gum tissue, to arrest caries and, with the aid of prophylactic measures, to cure pyorrhea and induce bone regeneration in the alveolar tissue. The Ca and P content of the blood varies with the age of the individual. Caries and bone absorption may be progressing rapidly in a person whose blood contains normal amounts of Ca and P. These processes have been stopped, by diet, without changing the blood values significantly.

HANZLIK, P. J. and D. A. WOOD (SAN FRANCISCO). **The Seat of Digitalis-Emesis.**

The mechanism of digitalis-emesis has been studied in pigeons which have been found useful in bio-assay of the drug. The results have been compared and correlated with those on mammals reported in the literature.

It was found that the emesis of digitalis in pigeons is peripheral in origin, the action consisting predominantly of a vagus-reflex mediated through local irritation by digitalis concentrated in the liver, other abdominal viscera not being excluded. The seat of emesis is not in the heart, a result which corroborates recently reported results in cats. The details are being published in the *Journal of Pharmacology and Experimental Therapeutics*.

HÁRI, PAUL (BUDAPEST). **Die Fehlerquellen spektrophotometrischer Bestimmungen.**

Zur Konzentrationsbestimmung von Farbstofflösungen, darunter auch solchen animalischer Herkunft, wurden spektrophotometrische Verfahren vorgeschlagen und auch vielfach verwendet. Nun sind zwar die Spektrophotometer, die zur Zeit gebaut werden, theoretisch glänzend durchdacht und auch technisch vollendet ausgeführt; doch erheischt ihr Gebrauch allergrösste Vor- und Umsicht; denn der Fehlerquellen, die das Resultat der Bestimmung unsicher machen können, gibt es so manche. So kann ein Apparat, der tadellos justirt und kalibriert wurde, und längste Zeit hindurch tadellose Resultate lieferte, später, ohne dass man es zunächst bemerken würde, falsche Zahlen geben, einfach aus dem Grunde, weil (vielleicht infolge kleinster Erschütterungen) gewisse verstellbare Bestandteile (Prismen) eine oft nur minimale Verschiebung erleiden, worunter natürlich die Justirung leidet. Zu falschen Resultaten kann auch ein unrichtiger Stand der Lichtquelle führen; denn, obwohl an vielen Apparaten diesem Fehler durch entsprechende Einrichtungen nach Möglichkeit vorgebeugt ist, kann beim Auswechseln des schadhafte gewordenen Glühkörpers ein Fehler in der Centrirung unterlaufen. Dass an Lösungen, die nicht ganz wasserklar sind, eine genaue spektrophotometrische Bestimmung nicht ausgeführt werden kann, ist allbekannt; weniger, dass kolloide Farbstofflösungen, auch, wenn sie kaum merklich opalisieren, fehlerhafte Resultate liefern. Wie so manchen Mitteilungen zu entnehmen ist, wird es wenig beachtet, dass in Farbstofflösungen, die vermöge ihrer Concentration oder vermöge der angewendeten Schichtdicke das Licht allzu stark bezw. umgekehrt allzu schwach absorbieren, der erhaltene Extinctionscoefficient mit unverhältnismässig grossen Fehlern belastet ist.

HARTMAN, FRANK and JAY I. EVANS (BUFFALO). The Control of Capillaries.

The skeletal muscle capillaries of the living cat have been studied by direct illumination under high magnification. The capillary walls could be distinguished. The sartorius muscle was observed.

Cutting the femoral nerve caused dilatation of the capillaries. Electrical stimulation of the cut nerve caused dilatation of the capillaries and if the stimulation was prolonged, constriction of the arteries and veins.

Stimulation of the abdominal sympathetic chain either intact or cut caused dilatation of the capillaries.

Reflex effects from stimulating the skin of the abdomen by electric shocks, by cold, or by heat caused dilatation of the capillaries of the sartorius. Mechanical stimulation of the pylorus caused dilatation of the capillaries of the sartorius.

Intravenous injections of the following substances caused dilatation of capillaries: Acetic, hydrochloric and lactic acids; acetyl choline, amyl nitrite (inhalation), atropine, calcium chloride, cocaine, ephedrine, epinephrin, ergotamine, ether (inhalation and local application), histamine; ammonium, potassium and sodium hydroxides; liver extract, nicotine, picrotoxin, pituitrin, and urethane (local application).

Hemorrhage even in small degree and completely compensated caused dilatation of the capillaries. Infusions caused dilatation.

Constriction of the capillaries was rare and difficult to produce.

In one cat, observed only with low magnification, stimulation of the femoral nerve caused the red cells to disappear. The capillary walls could not be seen, therefore the appearance might have been due to constriction of pre-capillary vessels. One experiment with sympathetic stimulation gave similar results.

Direct application of acetic acid caused constriction and injury of the capillaries.

Direct application of 1:10,000 epinephrin caused constriction or disappearance of capillaries. Doses of epinephrin as high as 1 cc. 1:10,000 injected intravenously caused dilatation of capillaries and venules but constriction of arterioles, veins and arteries.

Direct application of ethyl alcohol caused constriction of the capillaries.

Local application of two per cent ferric chloride caused constriction and injury of the capillaries.

In one cat, local application of ammonium hydroxide apparently caused capillary constriction.

The typical reaction of capillaries (mammalian skeletal muscle) to any but harmful stimuli is dilatation.

When erythrocytes disappear from the capillaries it seems to be due to constriction of precapillary vessels.

When new capillaries open in a field it may mean that precapillary vessels dilate and allow erythrocytes to enter vessels already open. We are unable to decide.

HARTMAN, F. W. (DETROIT). Effects of Reabsorption of Urinary Constituents from the Lower Ileum.

This is an experimental study carried out on dogs using a double anastomosis. First the ileum is divided in the middle portion and the ends inverted. The proximal portion is now anastomosed to the ileum just

above the caecum and the distal end is anastomosed to the fundus of the urinary bladder. In this way an easily controlled shunting of the urine into the bowel is produced without disturbing the ureters. Hydro-ureter, hydronephrosis and pyelitis are not encountered. The kidneys first hypertrophy often to twice the normal size and later show marked tubular degeneration and lipoidosis. The glomeruli are rarely affected up to the fifth month. The pathology, functional and vascular changes are contrasted with those observed in x-ray nephritis.

HARTMAN, F. W. (DETROIT). Effects of Cystoileostomy on the Kidneys. (Demonstration)

HARVEY, E. NEWTON (PRINCETON). The Effect of High Frequency Sound Waves on Cells and Tissues.

When a quartz crystal cut in a certain plane is compressed, it becomes charged + on one side,—on the other, the piezo-electric effect. Conversely, if a quartz crystal is charged + on one side—on the other, it will compress. Reversing the charges causes expansion. If the reversing of the charges is carried out rapidly by an oscillating electric field, sound waves of a frequency corresponding to the frequency of the oscillating field will be produced, which travel through a medium in contact with the crystal. Wood and Loomis (Phil. Mag. 4, 417, 1927) have described a high power (2 kilowatt) oscillator and Harvey and Loomis (Nature, 121, 622, 1928) a low power (75 watt) oscillator and crystal for use on the microscope. Frequencies of 300 to 2,500 kilocycles have been employed by the author in collaboration with Mr. A. L. Loomis to study effects on living cells. The sound waves cannot be heard but have definite mechanical effects. A drop of water is broken into a fine mist. *Elodea* cells show rapid whirling of the chloroplasts and breaking up of these bodies and the plasma membrane. Blood corpuscles are laked, provided they are not thrown into nodes of standing waves. Egg cells and infusoria are cytolysed, and the more easily the larger the cells. Bacteria can be broken up by high intensity sound waves and the suspension sterilized. Skeletal muscle, nerve, and luminous cells are not readily stimulated. Quiescent isolated turtle and frog ventricle can be made to contract with regular rhythm. Beating auricles will beat more rapidly. Small fish can be killed and the cause of death appears to be haemolysis and rupture of gill membranes. From the stirring of cell contents conclusions can sometimes be drawn regarding the viscosity of cells. No difference in effect can be detected with different frequencies.

HARVEY, E. N. (PRINCETON). The Effect of High Frequency Sound Waves on Cells and Tissues. (Demonstration)

HASTINGS, A. BAIRD and H. B. VAN DYKE (CHICAGO). Further Studies of Halide Distributions in the Blood.

A study has been made of the distributions of chlorides, bromides, and iodides between the serum and cells of blood. The results may be classified as follows:

1. Those in which halides are added to blood in vitro. In this case the distribution of the halides is not inconsistent with that predicted by the

Donnan equilibrium when allowance is made for slight differences in the activity coefficients of the ions.

2. Those in which halides are injected intravenously. The distribution in this case is not inconsistent with the *in vitro* results.

3. Those in which the halides are administered orally. Abnormally high distribution ratios are found soon after feeding bromides.

An attempt has been made to analyze the factors responsible for the apparent concentration of bromides within the cells.

HAUSWIRTH, L. (NEW YORK) and F. SILBERSTEIN (VIENNA). The Function of the Duodenum.

To answer the question whether the duodenum has any specific function, a method has been described that permits the whole duodenum to be resected and the ducts of the pancreas and the bile to be implanted in the jejunum. A specimen of a papilla thus healed into the jejunum is demonstrated. It originates from a dog that had survived the operation for more than a year. A number of dogs are said to be alive in very good condition for more than 1½ years since the operation. Succeeding observations of animals that have survived the operation for a few days or several weeks, are talked about.

The changes in the blood-picture and in the iron-content of the blood after the operation are discussed. Then the consequences of the removal of the duodenum for the metabolism of carbohydrates and proteins are discussed. Finally the sensibility of these animals against poisons is briefly related.

HAWK, PHILIP B. (NEW YORK). A Study of the Physiological and Psychological Reactions of the Human Organism to Coffee Drinking.

One hundred normal young men were selected from five hundred candidates and used as subjects in the investigation. Coffee was administered from one to three times per day over a prolonged period. The physiological and psychological responses of the subjects were determined at the start of the experimental period. Coffee prepared under controlled conditions was then fed the young men in stated daily quantities throughout varying periods of time. The men were then subjected to the same physiological and psychological tests as previously employed. The research schedule included a study of gastric digestion, kidney function and heart action together with a study of the response of the subjects to a number of standard tests in experimental psychology. The author concludes that:

The drinking of from two to six cups of coffee daily for a period of weeks or months by normal young men unaccustomed to its use had no outstanding deleterious action on the heart or circulatory system. There was, however, an increased pulse rate in several cases and cardiac palpitation and increased blood pressure in a few cases.

There was no outstanding or permanent interference with the gastrointestinal functions. There were, however, indications of gas formation, indigestion, diarrhea or constipation in about 50 per cent of the cases.

The kidney function was not deranged to any considerable degree. There was a mild diuresis in several cases and casts either made their appearance or increased in number in other instances.

The effect on blood urea and uric acid was variable.

The influence of coffee drinking upon the nervous system was very pronounced and unfavorable. This was indicated by a lessening of the period of sleep, a lowering of the quality of sleep (bad dreams), inability to concentrate, tremors or nervousness, headache and dizziness.

A further indication of a deranged nervous system was the less satisfactory response to certain psychological tests at the end of the coffee drinking period. Features which apply to a great majority of the cases investigated, are a *prolongation of the simple reaction time and a loss of accuracy in rapid calculating.*

The final conclusion is that coffee drinking as practised in these tests exerted no definite and prolonged deleterious influence upon the heart, kidney or gastro-intestinal tract. The nervous system was, however, very definitely and unfavorably affected and as a result, the mechanical and mental efficiency of the coffee drinkers was materially lowered and they became less efficient human machines.

The above conclusions also apply, with perhaps somewhat lessened force, to the influence of an increase (from one to three cups daily) in the coffee consumption of men who had taken coffee in moderate quantity for years.

HAYASHI, T., H. TAMURA and M. TAKEUCHI (TOKYO). **On the Nature of the So-Called Inhibition-Stage (Hemmungsstadium) of Narcosis Described by Wedensky (The Studies on Wedensky Effect, Part 5).**

In narcotizing experiments on nerve, after the conduction failed from an outside electrode, a strong electric stimulation of the narcotized region caused a muscle contraction which could be inhibited by the strong electric stimuli applied at the outside electrode. This stage of narcosis was called the "inhibition-stage" or the third stage (succeeding to the paradoxical stage). The present authors performed a series of experiments on this phenomenon, and reached the conclusion that the so-called inhibition-stage does not depend on the function of nervous impulses, but it should be attributed to the interference effect of stimulation currents spread beyond the narcotized region (which had already lost its excitability) to a certain distal point (X) which was still excitable. As one of the proofs for this inference the present authors pointed out the following fact:

If a subminimal stimulus is applied to a point (X) of nerve, it sets up of course no nerve impulse, but the point X suffers a marked change in its excitability: the threshold decreases for a very short time (2σ) immediately after stimulation and then increases. This increase, *i.e.*, inhibitory effect lasts fairly long ($2-12\sigma$). This effect is strictly localized in the stimulated point.

In the so-called inhibition-stage, the strong electric stimulus applied at the outside electrode spreads to the distal point X and leaves there an inhibitory effect. This inhibitory effect inhibits the inside stimulus from exciting the point X. If we narcotize a sufficiently long stretch of nerve, the so-called inhibition-stage can never be observed, because the point X is beyond the reach of current spread from the outside electrode.

HECHT, SELIG, ERNST WOLF and GEORGE D. WALD (NEW YORK). **The Visual Acuity of Insects. (Cinematograph Demonstration)**

A method has been devised for measuring the visual acuity of animals other than man by using the characteristic responses which animals make

to a movement in their visual field. This has been used to study the relation between illumination and visual acuity in the insect eye, which is structurally different from the vertebrate eye. Experiments with the bee and with *Drosophila* show that their maximum visual acuity is lower than the lowest human acuity. Under similar maximal conditions human visual resolution is about 100 times that of the bee and over 1000 times that of *Drosophila*.

The insect eye is a mosaic of hexagonal pyramids of differing apical angle, which determines the separation of adjacent ommatidia. The minimum visual angle which the bee can discriminate as measured experimentally is identical with the minimum angular separation of adjacent ommatidia as found structurally. If this region of minimum ommatidial separation is painted out, the maximal visual acuity then corresponds to the angular separation of the remaining ommatidia.

The visual acuity of the bee and of *Drosophila* varies with the illumination in much the same way that it does for the human eye. It is low at low illuminations; as the intensity of illumination increases it increases; and finally at high intensities it becomes constant. The resolving power of a structure like the insect eye depends on the distance which separates the discrete receiving elements. The data then mean that at low illuminations the distance between receiving elements is large and that this distance decreases as the illumination increases. Since such a moving system cannot be true anatomically it must be interpreted functionally. It is therefore proposed that the threshold of the various ommatidia are not the same but that they vary as any other characteristic of a population. The visual acuity will then depend on the distance apart of those elements whose thresholds are such that they are functional at the particular illumination under investigation. Taking due consideration of the angular separation of ommatidia it is possible to derive a distribution curve for the thresholds of the ommatidia which resembles the usual probability curves, and which describes the data with complete fidelity.

HÉDON, L. (MONTPELLIER). **Tentative de démonstration "in vivo" de la glyconéogénie aux dépens de la graisse.**

La formation dans l'organisme de substances hydrocarbonées aux dépens des acides gras est niée par les uns, considérée au contraire comme possible par d'autres, sans qu'une preuve décisive en ait encore été apportée. La valeur du rapport D:N dans le diabète ne démontre pas cette formation d'une manière certaine, pas plus que la valeur du Quotient respiratoire. Les valeurs très basses du Q. R. chez les animaux hibernants n'ont pas été confirmées par les expériences récentes, et dans le diabète, le Q. R. ne descend jamais fortement au dessous de 0,7.

Si des hydrates de carbone se forment réellement aux dépens des acides gras, on peut supposer que c'est par une réaction couplée avec une combustion de sucre. Cette hypothèse expliquerait que le Q. R. reste voisin du quotient de combustion des graisses. Des expériences ont été faites pour la mettre à l'épreuve et pour chercher à dissocier la glyconéogénie de la combustion du sucre.

Des chiens totalement dépancréatés et maintenus à jeun pendant plusieurs jours ont reçu sous la peau des injections de phlorizine en quantité suffisante pour ramener leur glycémie à un niveau voisin de 1 p.1000 et

pour essayer par là de diminuer la combustion du sucre, puis des injections sous-cutanées d'adrénaline pour porter la glycosurie à un niveau très élevé. Dans ces conditions des rapports D:N atteignant 13, et même 14,7 ont été observés dans l'urine. Une expérience d'échanges gazeux pratiquée au moment de l'élévation maxima du rapport D:N a donné un Quotient respiratoire de 0,648. La réserve alcaline du plasma n'avait pas changé pendant cette expérience.

La coïncidence d'un rapport D:N très élevé et d'un Q. R. notablement inférieur au quotient de combustion des graisses est un argument en faveur d'une formation de sucre aux dépens de substances non azotées et pauvres en oxygène. La complexité des conditions expérimentales interdit cependant toute conclusion définitive.

HEMMINGSSEN, A. M. (GENTOFTE). Attempts of Inducing Mating Instincts in Spayed Rats and Mice with Ovarian Extracts.

Out of 35 sprayed rats in which cornification of the vaginal epithelium was induced by injection of ovarian extracts and which were placed together with aggressive males and inspected at proper intervals only two showed deposition of vaginal plugs. Different oily and watery solutions were employed for injection. The positive results were obtained by following a number of injections of oily solutions by watery but other experiments carried out in a similar way were negative.

Out of eight sprayed mice injected with ovarian extracts four showed deposition of vaginal plugs but plugs were also observed in three sprayed mice which had not been injected. In most cases plugs were inserted in the mice although examination of the vaginal smear a few hours before or on the day before had given no evidence of an approaching oestrous period. It was impossible to get smears from a vagina containing a plug. Histological examination of the ovarian region of the rats and mice showing plugs revealed no tissue accounting for the mating except perhaps some tissue resembling luteal cells in one of the rats.

The proportion of copulatory results reported by other investigators are in one case greater (Allen and co-workers) in most cases (Parkes, Fielding and Bellerby, Asdell and Marshall, Oslund, Evans and Burr) less than found by the author.

The impression gained from the facts presented and from other publications is that cornification of the vaginal epithelium cannot be considered a reliable criterion of heat in spayed animals, and there is so far no definite proof that the hormone producing oestrous growth is responsible for the phenomenon of heat, except perhaps when certain unknown conditions are prevailing.

HENDERSON, YANDELL (NEW HAVEN). An Improved Apparatus for Measuring the Circulation in Man by Means of Ethyl Iodide, Carbon Dioxide or Other Gases. (Demonstration)

HERNANDEZ, EUSEBIO ADOLFO (PARIS). On the Necessity for Having Special Laboratories for the Experimental Study of Somatic Death.¹

Prof. A. Kouliabko proposed to us, more than a year ago, that we should collaborate with him in the formation of an international organization of physiologists for the experimental study of death.

¹ E. Gley, *Le problème de la vieillesse devant la physiologie d'aujourd'hui*, La Revue de France, Paris 1er septembre 1924.

The sole purpose of this paper is the justification of this idea of the Russian physiologist—an idea with which we are in complete agreement.

Only a physiologist like Kouliabko, who has made such admirable experiments on the survival of the human heart (30 hours after death), could have the necessary appreciation of this problem and of the technique therefor.

The problem of death. From the point of view of physiological "determinism," death is, in general, an avoidable phenomenon. "Knowledge is power."

Experimental thanatology. The study of death, from the medico-legal aspect, is not a physiological investigation. As a physiological study it would be the investigation of the mechanism of somatic death.

Conservation of life in an organism already created, is something quite apart from the problem of the artificial creation of life, the dream of Jacques Loeb.

Classical physiology and the study of death. Classical physiology has not approached the question of death in a methodical and direct fashion.

When, for example, Cl. Bernard asked himself what is the cause of death in a dog or a rabbit after double cervical vagotomy, he said: "We are going to see how the animal dies," and the possible cause is nothing more than an "interpretation."

On the other hand, Professor Pavloff began his experiments at the point where Cl. Bernard left off. He did not ask himself "How does one die?" but "How can one still live after such a cause of death?"

It is true that Cl. Bernard himself sometimes followed this line of seeking to prolong life after different causes of death. For example, in the case of "curare," administered to animals who were then submitted to artificial respiration, which can prevent death in the higher animals after curare. But these are isolated experiments, for no systematic research has been made by the classical physiologists.

Magendie, so insistent upon facts in other realms of physiology, contents himself always with "explanations" when the cause of death of the subjects of his experiments on the nervous system, is in question.

One might think that death was not in the reach of experimental physiology, were it not for some well-known exceptions (isolated head-preparation of Brown-Sequard, abdominal respiration of E. Wertheimer, etc.). And that is why today the study of isolated organs from the point of view of classical physiology, is only just beginning.

Survival of isolated organs. We are beginning to take the trouble to perfect the technique of isolated organs. So far, there has been a tendency to apply different techniques which are not yet satisfactory in themselves. For example, the technique of the isolated head, devised by Prof. J. P. Heymans, published in 1912, permitted a survival of 2 to 3 hours. And today, with this technique, we are still at the same point, as we had occasion to observe at the Physiological Congress at Stockholm.

The fault lies, not with the present research-workers, but rather with our impatience to apply these methods, and our present scorn of classical physiology and its aims. We are more ambitious, it seems: We demand a physico-chemical explanation of the phenomena of life, and we neglect the patient study of the special mechanisms of the higher animals.

The limits of general physiology. Today the experiment of the isolated-head or other study of an organ in condition of survival, is not by itself

in the domain of general physiology. On the contrary, Cl. Bernard in his book "*De la Physiologie Générale*" speaks of this experiment by itself, that is to say, without any special application, and he sees its general bearing—a point of view too often forgotten.

The fatalism of death in modern biology. Such workers as Weismann, in an epoch wherein one could not make experiments but merely made hypotheses about the mortality of the somatic cells, ascribed the death of the higher organisms to a "natural law."

This historical lesson should teach us to mistrust scientific fatalism arising so easily from a single observation and disappearing when experimental investigation begins.

Physiological resurrection. The term "resurrection," absolutely provisional, has been employed in the United States by Prof. G. N. Stewart and his co-workers. Stewart, who is not very optimistic in his conclusions, propounds the following question: Why can we not do with the complete organism what we can do with certain portions (survival of isolated organs).

The reservations of Professor Stewart are not however insurmountable. Prof. O. Zeller has undertaken, like Brown-Sequard, experiments on resurrection, and has succeeded, to a certain extent, in re-establishing the general circulation.

With regard to respiration, the experiments of E. Wertheimer have opened out a path which we have essayed to follow in the laboratory of Professor Pugliese at Milan, to obtain abdominal respiration in a dog, without the intervention of the respiratory centre of Flourens, some hours after the section of the cord, between the atlas and axis. The results have not been altogether negative, in regard to diaphragmatic contractions.

The problem of death is not only the problem of the conservation of life. It also includes the problem of the preservation of "consciousness," that is to say of our "associative memory," a truth clearly perceived by Lucrece when he formulated the problem of death scientifically.

A decerebrate dog can certainly *live*; but we require also the conservation of our brain, in order to preserve at the same time our intellect.

To measure the resistance of the brain to a total anemia, *i.e.*, to death, the following points are requisite: First, that the anemia artificially produced shall be total; secondly, that, after this anemia, it shall be possible to reestablish the cerebral circulation in a suitable manner. Both these conditions are fulfilled by the isolated head-preparation shown by us in a film at the Academy of Medicine, at Berlin: The head, separated from the body, retains the phrenic nerves (for respiration) the vago-sympathetics, the carotids, vertebrals and jugulars. The rest of the neck, even the spinal cord, is divided in the region of the seventh cervical vertebra, which allows of an absolute control of the cerebral circulation.

Such a circulation in a dog sufficed for a survival of 13 hours.

To sum up: It is necessary to coördinate these experiments, to arrive at a control of the mechanism of death. The experiments are important enough also from the point of view of surgery and may possibly lead us to the site of origin of the causes of old age.

Therefore, we need special centres for the physiological researches of experimental thanatology in which, without explaining the phenomena of life, we may prevent those of death.

HERZFELD, E., L. VALLAGNOSC, et J. GAUTRELET (PARIS). **Action de l'aldéhyde formique sur la respiration (apnée) et la réserve alcaline.**

Nous avons constaté que l'injection intraveineuse de 2 et 3 centigrammes par kilogr. d'aldéhyde formique chez le chien chloralosé provoquait en même temps que la baisse de pression et le ralentissement cardiaque (O. Vechiu et J. Gautrelet) une apnée plus ou moins durable suivie d'une hyperpnée prolongée.

L'apnée paraît avant tout d'origine périphérique: il suffit de sectionner les vagosympathiques pour qu'elle disparaisse généralement; à dose suffisante, cependant, une phase apnéique, plus prolongée même, peut parfois se manifester mais son apparition est moins immédiate.

Ayant effectué la mesure de la réserve alcaline, nous avons constaté que les variations trouvaient logiquement leur explication dans les variations du rythme respiratoire et de la pression sanguine: la R. A. augmente parfois très légèrement (5%) au cours de l'apnée, elle diminue ensuite progressivement (10 à 20%) au cours de l'hyperpnée et de la chute de pression, après la section des vagosympathiques notamment, jusqu'à 30%.

L'injection préalable d'yohimbine ne supprime pas l'apnée.

Enfin nous avons constaté que sous l'influence d'une respiration artificielle modérée mais ne permettant pas à l'animal le contrôle de ses mouvements respiratoires, et par conséquent supprimant l'apnée, l'injection d'aldéhyde formique provoquait les modifications habituelles de la R. A. mais manifestait une toxicité plus accusée (double parfois) que normalement.

Nous n'avons pas constaté de modification digne d'intérêt du pH sous l'influence de l'aldéhyde formique.

HESS, W. R. (ZÜRICH). **The Mechanism of Sleep.**

All the existing hypotheses concerning sleep have proved to be unsatisfactory, seeing that they are insufficiently supported by the known facts regarding sleep. The researches here referred to are intended to supplement hypotheses. After developing a special method in which the kind of electrical impulse and the shape of the electrodes play an essential part, an inhibitory state was induced as a consequence of electric excitation of a certain part of the brain, which exhibits the following signs of physiological sleep: correct sleeping position, retention of the aural titillation reflex, contraction of the pupils, adequate attitude to waking excitations, and above all the characteristic temporal course of all the symptoms. (Illustration by film; reference to separate demonstration of a method film.)

This finding shows us that sleep is the consequence of a *state of excitation* of certain portions of the central nervous system. This is the one side of the results of our researches; the other arises out of the histological control of the brain for the purpose of localizing the parts inducing sleep. These were *not* encountered in a narrowly confined sphere (in the sense of a circumscribed sleep-centre). Their distribution, however, is regular in as far as they are localized along the axis of the brain and adjacent to the ventricles. In the influence of these deep strata on higher brain parts, in the sense of regulation of the readiness to function, we perceive something fundamental concerning the functional structure of the central nervous system.

With regard to the sleep problem we would point out the characteristic that the effective excitatory parts lie in the same strata for which regulatory relations to the vegetative functions are assumed.

This finding will be more clearly understood if we perceive as nucleus of the sleeping process not the *negative*, i.e., the extinction of functional potencies, but the *positive*, i.e., the promotion of restorative processes within the tissue. As the regulation of interior bodily conditions belongs to the sphere of the vegetative functions, the mechanism of sleep is on a level with the vegetative reflex-functions.

HESS, W. R. (ZÜRICH). **Methodik der Reizung und Ausschaltung subcortikaler Gehirnabschnitte.** (Kinematographische Demonstration)

HEUBNER, WOLFGANG (DÜSSELDORF) und FRIEDRICH HOLTZ (GÖTTINGEN).

Untersuchungen über bestrahltes Ergosterin.

Durch ultraviolette Bestrahlung von Ergosterin unter *völligem* Sauerstoffausschluss wurden mehrere Isomere dargestellt, darunter das Vitamin D. Ferner wurden verschiedene Präparate in ölgiger Lösung, die in wissenschaftlicher Laboratorien oder von industriellen Firmen durch Bestrahlung mit kurzwelligem Licht aus Ergosterin gewonnen waren, in ausgedehnten Versuchsreihen an Ratten, Kaninchen und Hunden geprüft. Dabei handelte es sich einmal um einen Vergleich von Präparaten verschiedener Herstellung in Bezug auf das darin enthaltene Quantum wirksamer Substanz, und zwar sowohl in Bezug auf die Heilwirkung bei experimenteller Ratten-Rachitis wie auf die vergiftende Wirkung bei gesunden Tieren; zweitens handelte es sich um den Vergleich der Heilwirkung mit der toxischen Wirkung, insonderheit um die Frage ob beide in einem konstanten Verhältnis stehen, also mutmasslich der gleichen Substanz zuzuschreiben sind. Alle Versuch sprachen für Bejahung dieser Frage. Die Giftwirkung wurde im einzelnen studiert, vor allem die degenerativen, zur Verkalkung führenden Prozesse in den Blutgefässen in ihrer Entstehungsweise verfolgt. Es konnte mit Sicherheit eine allgemeine Wirkung auf den Kalzium- und Phosphatstoffwechsel von einem unmittelbaren, degenerativ wirkenden Einfluss auf das Gewebe unterschieden werden. Bei subcutanen Injektionen wurde beides auch lokal im Gewebe beobachtet.

HEYMANS, C. (GAND). **Recherches sur la physiologie et la pharmacologie du sinus carotidien.**

Le sinus carotidien d'un chien B est isolé et anastomosé dans la circulation carotido-jugulaire d'un chien A; seul le nerf intercarotidien relie le sinus perfusé de B aux centres encéphalo-bulbaires de B.

Cette méthode, associée aux méthodes expérimentales de la tête "isolée" d'après J. F. Heymans et ses élèves, de l'anastomose surrénalo-jugulaire d'après Tournade et Chabrol, de la perfusion de la rate d'après Sollmann et Pilcher, de la perfusion du rein d'après Tournade, permet de démontrer que:

a. les variations physiologiques de la pression artérielle chez A, perfuseur du sinus "isolé" de B, reproduisent chez B les ondes vasomotrices de Traube-Hering.

b. d'accord avec H. E. Hering, le sinus carotidien est une zone vasosensible et réflexogène, régulatrice du tonus vago-sympathique cardiaque et du tonus vasomoteur en rapport avec la pression artérielle.

c. l'hypertension dans le sinus carotidien "isolé" de B réalisée par l'injection de Ringer, d'adrénaline, d'éphédrine ou de pituitrine au perfuseur A, déclenche de la bradycardie, de la vasodilatation et de l'inhibition de l'adrénalino-sécrétion chez B.

d. l'hypotension artérielle dans le sinus carotidien "isolé" diminue progressivement le tonus physiologique cardio-vaso-et adrénalino-dépresseur du nerf intercarotidien de H. E. Hering.

e. l'adrénalino-sécrétion est réglée, d'une manière réflexe et continue, par la pression sanguine qui agit sur les zones vasosensibles de l'aorte et des sinus carotidiens.

f. le tonus des vaisseaux céphaliques [cérébraux (H. S. Forbes et H. G. Wolff)], s'adapte d'une manière réflexe à la pression artérielle aortique et carotidienne.

g. l'adrénaline agissant uniquement au niveau du sinus carotidien intensifie les réflexes partant de cette zone vasosensible.

h. le volume de la rate est réglé d'une manière réflexe par la pression artérielle agissant au niveau des sinus carotidiens.

Appliquant dans une même expérience la méthode de perfusion par un chien A du sinus carotidien "isolé" d'un chien B et la méthode de perfusion de la tête "isolée" de B par un chien, on démontre que ni l'hypertension, ni l'hypotension, ni l'adrénaline, ni l'éphédrine agissant uniquement sur les centres encéphalo-bulbaires de la tête "isolée" de B ne provoquent de réactions cardiaques ou vasomotrices chez le tronc B, tandis que les mêmes agents physiologiques et pharmacologiques portant uniquement leur action sur le sinus carotidien "isolé" de la tête B déclenchent chez le tronc B, par la voie réflexe du nerf intercarotidien, toutes les modifications cardiaques, vasomotrices et adrénalino-sécrétoires qui sont généralement attribuées à une action directe sur les centres.

HEYMANS, C., BERTHE HEYMANS et JEAN J. BOUCKAERT (GAND). **Démonstration, par la méthode de la perfusion du sinus carotidien "isolé" ou de la méthode de la perfusion de la tête "isolée," que le sinus carotidien est une zone réflexogène régulatrice de la fréquence de coeur, du tonus neuro-vasculaire et de l'adrénalino-sécrétion.**

HEYMANS, C., BERTHE HEYMANS et JEAN J. BOUCKAERT (GAND). **Hyperthermie jusque 45° chez le chien par injection intraveineuse de bleu de méthylène, d'azur de méthylène, de dinitronaphthol, de thionine, de bleu de toluyène. (Démonstration)**

HILL, A. V. (LONDON). **The Heat-Production of Crustacean Nerve.**

Levin described a "retention of action current," lasting many minutes after stimulation, in the non-medullated limb nerves of *Maia* and other crustaceans. These nerves are readily fatigued, and their recovery from fatigue is associated with the disappearance of Levin's "retention." Furu-sawa has shown recently that the restoration process occurs only in the presence of oxygen, and has proved that the "retention of action current" is really to be regarded as a "diminution in injury current," i.e., as a decrease in the degree of electric polarization normally existing at the surface of the nerve fibre.

It has proved possible, simply with thermopile and galvanometer (without amplification), to measure the rate of heat-production of *Maia* nerves for 30 minutes after a 5- or 10-second tetanus. Nearly the whole of the heat (about 98 per cent) is liberated in recovery. The rate of recovery heat-production rises rapidly to a maximum, and then falls slowly to zero in about 30 minutes at 13°C. The course of the recovery process is analogous to that occurring in stimulated muscle.

The existence of this important recovery phase, and its time-relations, confirm the view that the gradual disappearance of the "retention of action current," the gradual "repolarization" of the nerve after a stimulus, are essentially a restorative, "recharging" process, the energy for which is supplied by oxidation.

HILL, R. L. (LOGAN, UTAH). Soft-Curded Milk—A Modern Solution of the Difficult Feeding Problems with Infants.

A test has been developed at the Utah Agricultural Experiment Station by which the toughness of the curd formed by the normal coagulation of milk can be measured. It has also been demonstrated that the results obtained from the use of this test is a direct index to the digestibility of the milk by infants.

A wide range has been demonstrated in the toughness of the curd and resultant digestibility of milk from different cows in the same and different breeds of dairy cattle. Results also indicate that on the average not more than 10 per cent (and in many cases a lower percentage) of the cows give milk that is soft-curded enough for the use of delicate infants. The results obtained by feeding the milk to infants would indicate that the toughness of the curd of the milk is far more important than the fat content in choosing a milk for infants. By the use of the curd test on the milk from a large number of individual cows, a soft-curded milk may be obtained. It is possible to obtain soft-curded milk with either a high or low fat content. It is also possible to obtain cows' milk that closely approaches human milk in its digestibility by infants. Such milk, when fed to infants, requires little, if any, dilution or modification.

HIMWICH, HAROLD E. and L. H. NAHUM (NEW HAVEN). Respiratory Quotient of Brain.

The respiratory quotient of the brain has been studied by analysis of samples of blood entering and leaving that organ for carbon dioxide and oxygen. In 38 observations on 14 dogs, 5 of which were normal, (4 under amytal anaesthesia and 1 without any general anaesthetic), and 9 diabetic (4 phlorhizinized, 4 depancreatized and 1 both phlorhizinized and depancreatized), the average of the respiratory quotients of the brain was 1.00. The respiratory quotients obtained from the expired air corresponded with the nutritive conditions of the animals, and in the diabetic dogs varied between 0.67 and 0.71.

The glucose and lactic acid contents of samples of arterial and venous blood were also studied. A diminution of either or both of these substances might be expected in the blood passing through the brain since its store of carbohydrates is exceedingly small. Taking into consideration only the significant determinations i.e., those which yielded differences of 5 mgm. per cent or more we found in 25 such observations on normal dogs that the brain removed glucose in every instance and removed lactic acid in 8 of 12 cases. The brains of the diabetic dogs took out glucose from the blood

traversing it 14 times in 17 observations and did the same for lactic acid in 7 of 9 determinations.

HIRSCHFELDER, ARTHUR D. (MINNEAPOLIS). The Antagonism of Potassium and Sodium Ions to the Narcotic Effect of Magnesium, and Its Relation to the Physical Chemistry of Narcosis.

Meltzer and Auer found that magnesium salts subcutaneously or intravenously produce narcosis and anaesthesia, and that animals with magnesium can be instantly awakened by calcium salts. In series of experiments to be reported, the same sudden awakening can be brought about by potassium or rubidium chloride. Very large amounts of sodium chloride have a similar but less marked effect. Lithium chloride is still less active; ammonium chloride not at all. The relation of these effects to their physico-chemical effects on emulsions and suspensions of lipoids is considered in relation to the problem of narcosis and cell activities. Other anaesthetic, narcotic and analgesic drugs have the same effects on emulsions as have magnesium salts.

HIRSCHFELDER, ARTHUR D. and H. N. G. WRIGHT (MINNEAPOLIS). Physico-Chemical Studies Upon Antisepsis and Chemotherapy.

An attempt has been made to learn something about the fundamental physico-chemical phenomena involved in the actions of antiseptics and chemotherapeutic drugs. A number of the principal antiseptic dyes usually thought to be dissolved as crystalloids, are found to be partly crystalloid and partly in the colloid state, and some which are crystalloidal in pure water, become partly colloidal in physiological salt solution. The diminution in activity of antiseptics in the presence of proteins is due to adsorption on the protein rather than to chemical combination, but the portion of the antiseptic adsorbed on the protein seems to exert some antiseptic effect as well as does the dye that remains unadsorbed. The interference of one dye with the therapeutic action of another found by Schnitzer in the treatment of rats infected with trypanosomes, can be reproduced in the test-tube in the effect of triphenylmethane dyes and acriflavine on yeasts. Mercurochrome injected intravenously in animals stains the blood plasma pink, but this pink plasma will no longer fix itself to yeast or bacteria cells, as does the dye from an aqueous solution; hence the markedly decreased bactericidal action. On the other hand, the dyes cause the aggregation of protein particles, which explains clinical toxic reactions. All these experiments furnish points of attack for the study of the fundamental phenomena involved in antisepsis and chemotherapy.

HITCHCOCK, F. A. (COLUMBUS, OHIO). Variations in the Basal Metabolic Rate Apparently Caused by the Mental State of the Subject.

M. C. is a woman about thirty years old. She was a subject for metabolism tests over a period of about three months. During the first half of this period she took the series of oral and written examinations that are required of all students before they are admitted to candidacy for the degree Doctor of Philosophy. The average of 18 tests made on her before these examinations were completed was 40.12 Cal. per sq. m. of body surface per hr. Eight additional tests were made on her over a period of four weeks after all her scholastic work had been finished. These averaged 35.89 Cal. per sq.m. of body surface per hr., a drop of 10.5 per cent

from her previous level. The mental let-down which naturally accompanied the successful completion of her examinations is the only apparent cause for this decrease in the metabolic rate.

F. R. is a woman in her early thirties. During the spring of 1928 her basal metabolism was being determined daily. At this time she was a junior in the college of medicine. On the morning of June 1, the second day of her menstrual period, her B.M.R. was 31.95 Cals. per sq. m. of body surface per hr. The average of 54 tests run on this subject during menstrual periods was 32.60 Cals. On the evening of June 1 she was on duty for the first time at the University Dispensary and returned to her room very much excited by this experience. The following morning she had a metabolic rate of 42.35 Cals. per sq.m. of body surface per hr. On June 4 it was down to 33.23 Cals. The only explanation that can be offered for this temporary increase is the mental state of the subject.

Several other similar cases have been noted.

HÖBER, RUDOLF (KIEL). Die Konzentrierungsarbeit der Tubulusepithelien in der Froschniere.

1. *Farbstoffe.* Sulfosäure-Farbstoffe, welche von der vena portae renalis aus der Niere zugeführt werden, werden nur dann in die Harnkanälchen durchgelassen, wenn sie einigermaßen lipoidlöslich sind, während lipoidunlösliche Farbstoffe, soweit sie nicht ausgesprochen kolloidal sind, nur von den Glomeruli aus in den Harn gelangen können. Die lipoidlöslichen Farbstoffe werden in den Epithelien der Tubuli gespeichert und bei ihrem Uebergang in die Harnkanälchen eventuell sehr stark (z. B. 50 fach und mehr) konzentriert abgeschieden. Die lipoidunlöslichen Farbstoffe werden dagegen nur wenig (2-4 fach) konzentriert; des geschieht durch Wasserrückresorption.

2. *Harnstoff.* Der Harnstoff, der ebenso stark konzentriert wie die lipoidlöslichen Farbstoffe abgeschieden wird, verhält sich auch sonst ähnlich den Farbstoffen. Wie Marshall und Crane zuerst zeigten, wird der Harnstoff in den Epithelien der Froschniere gespeichert. Dieser Speicher wird dann aktiv von den Zellen entleert. Gewöhnlich verkleinert sich das Harnstoffdepot bei der Durchströmung der Niere mit Ringerlösung durch Uebertritt in den Harn; das entleerte Depot kann man dann von der vena portae aus von neuem auffüllen. Die Füllung und Entleerung des Depots lässt sich durch Narkotika und durch Cyanid hemmen. Im Winter geben die Epithelien keinen oder nur sehr wenig Harnstoff aus ihrem Depot ab.

HOCHREIN, MAX (LEIPZIG). The Effect of Lactic and Carbonic Acids on the Affinity of Hemoglobin for Oxygen. Investigation in association with D. B. DILL, J. H. TALBOTT, H. T. EDWARDS and L. J. HENDERSON (BOSTON).

We are indebted principally to Barcroft and his associates for our knowledge of the quantitative effect of change in acidity *in vitro* upon the affinity of hemoglobin for oxygen. With the methods of blood gas analysis developed by Van Slyke and his associates, it has become possible to extend the boundary of our knowledge in this field.

It has been found in diabetic coma that the rate of change of position of the oxygen dissociation curve of whole blood with pH, is not linear as in normal blood but decreases with increasing alkalinity, especially on the

alkaline side of $pH_e = 7.0$.¹ Since this phenomenon may be related to change in character of hemoglobin itself, experiments have been carried out on normal and acidified blood, equilibrated with carbonic acid and oxygen. Seven specimens of blood from M. H. and J. H. T. were employed. Lactic acid concentration was varied from 1 to 34 millimoles per liter and each specimen of blood was equilibrated with 40 millimeters pCO_2 and variable pO_2 values. The pH_e value for each point on the oxygen curves was calculated by interpolation on the carbonic acid dissociation curves. Thus, by a method of successive approximations, a set of oxygen dissociation curves for each subject was drawn. The results show a relation between pH_e and $\log pO_2$ at half saturation much the same as that found when acidity is varied by carbonic acid changes alone.

In another experiment a single specimen of horse blood was divided in two portions. One portion was equilibrated with oxygen and with carbonic acid pressures which gave a pH_e range from 6.32 to 7.63. The other was equilibrated with similar gas mixtures after acidification with lactic acid, 33 millimoles per liter, making possible a comparison of effects of lactic and carbonic acids over a wide range of acidity and on the same specimen of blood.

In normal blood, pH_e bore a linear relation to $\log pO_2$ at half saturation between the experimental limits of pH_e . In acidified blood there was less change in position of the curve for a given change in pH_e and the rate of change decreased with increasing alkalinity. It thus appears that the condition found in diabetes is related to ionic environment rather than to change in character of hemoglobin.

A study was made of sodium and potassium concentration in serum and cells of the same specimen of horse blood before and after addition of lactic acid. This will be reported more in detail elsewhere; it is simply noted here that addition of 33 millimoles of lactic acid per liter of blood resulted in migration of about 1 millimole of sodium and of potassium.

HOCKETT, A. J. and C. H. THIENES (PORTLAND, OREGON). The Reciprocal Activity of the Muscle Coats of Guinea Pig Intestine.

By use of a modification of the Trendelenberg method for the study of excised guinea pig intestine, there was demonstrated a coördinated reciprocal activity of the longitudinal and circular muscle coats of duodenum, jejunum and ileum. In seventeen of twenty-four segments of intestine, contraction of the longitudinal muscle was accompanied by relaxation of the circular muscle, and vice versa. Four of the remaining seven segments developed reciprocal activity after treatment with atropine and nicotine. Epinephrin relaxed the circular muscle and increased the tonus of the longitudinal; barium chloride and pilocarpine contracted the circular muscle and relaxed the longitudinal, in a majority of trials.

HOET, J. C. (LOUVAIN). On Traumatic Shock and Death by Burns.

It has been attempted to class in the same pathogenic group the circulatory conditions in traumatic shock, "shock" by burns, and histamine toxemia.

Simonaet and myself were unable to substantiate that hypothesis. We

¹ D. B. Dill, A. V. Bock, J. S. Lawrence, J. H. Talbott and L. J. Henderson. Journ. Biol. Chem., lxxi, 551 (1929).

first studied the "experimental traumatic shock" as produced by Cannon and Bayliss.

A strong traumatization of the hind limbs gives an immediate progressive fall of blood pressure, which has been called "experimental traumatic shock." There is no proof that this condition is due to some toxemia.

An intact innervation is absolutely necessary for the development of the lowering of the blood pressure. There is never in any case a concentration of the blood.

Scalding produces an immediate concentration of the blood in the etherized animal and produces a general capillary dilatation in the viscera, although they had not been submitted to direct influence of a rise in temperature.

Cutting the spinal cord completely modifies the immediate symptoms of scalding.

We reach the conclusion that "experimental traumatic shock" and the "shock" of scalded animals are two completely different circulatory conditions.

HOFFMANN, PAUL (FREIBURG I.B.). Ergebnisse der Untersuchung der Atemreflexe mit Hilfe der Aktionsströme.

Die Untersuchung der Aktionsströme des Zwerchfells und des N. Phrenicus bei gewöhnlicher Atmung ist mehrfach durchgeführt worden. Zur Untersuchung der Atemreflexe hat man sich dieses Mittels aber noch nicht systematisch bedient. Es gelingt in dieser Weise einige Aufschlüsse zu erhalten, die über das Bekannte hinausgehen. Die Selbststeuerung der Atmung ist eindringlich zu demonstrieren. Es lässt sich zeigen, dass die Einwirkung der Aufblasung und Ansaugung mit sehr kurzer Latenz einsetzt (wenige 1/100 Sekunden) und dass die Wirkung während des im Gange befindlichen Atemzuges eintritt, der je nachdem verkürzt, verstärkt, unterbrochen wird. Die Abhängigkeit von der Ventilation ist sehr deutlich. Bei Apnoe werden die Reflexe für Ansaugen aufgehoben, die Wirkung des Aufblasens kann sich bei geschlossenem Thorax und intensiver Hyperventilation ins Umgekehrte verwandeln. Bei noch stärkerer Ventilation verschwindet jede reflectorische Wirkung. Die Wirkung der V. Reizung ist ebenfalls abhängig von der Ventilation, bei Apnoe tritt gar keine Wirkung ein. Die Atmungsmuskulatur wird jedesmal auf diejenige Stellung eingestellt, die der Expiration entspricht. Bei elektrischer Reizung des zentralen Vagusstumpfes kann man feststellen, dass die einzelnen Erregungen durch das Zentrum hindurch nach dem Zwerchfell laufen mit sehr kurzer Latenz der Übertragung (0,015 Sek.). Die Erregungen passieren das Zentrum regelmässig, wenn das Zwerchfell sich in mässiger Erregung befindet; bei Dyspnoe in der Expirationsphase, wenn das Zwerchfell völlig erschlaft ist, findet kein Durchlaufen statt. Es ist also eine gewisse Bahnung notwendig, wie dies von den spinalen Reflexen bzw. den Eigenreflexen bekannt ist. Man kann feststellen, dass das Zentrum für das Durchlassen dieser Erregungen eine Refraktärperiode besitzt, die ziemlich kurz ist; (absolut refraktäre Periode bei mässigem Reize ca 2/100 Sekunden).

HOGAN, ALBERT G. and CHARLES L. SHREWSBURY (COLUMBIA, MISSOURI).

The Nutritional Requirements of the Chick.

Several attempts at obtaining normal growth of chicks on rations of simplified nutrients have been described, but without exception all of them have ended in failure. Our experience is that in many cases very slow growth is the only abnormality, in others the symptoms suggest polyneuritis. Our first attempts at supplying additional vitamin B did not lead to success. Some of the chicks received skim milk to drink, instead of water, and consumed large amounts. Others received supplements of the Osborne-Wakeman vitamin B concentrate. In both instances the chicks grew very rapidly for two or three weeks, but after that time many of them would suddenly collapse, with the symptoms commonly associated with synthetic diets. It seemed impossible for a single substance to be present in these supplements in sufficient quantity to increase the rate of growth, and at the same time in so inadequate a quantity as to permit the development of polyneuritis. For the time, therefore, we discarded the idea that the symptoms were due to a deficiency of vitamin B.

Somewhat later we weighed the internal organs of chicks receiving simplified diets, and made blood analyses. The adrenal glands were much enlarged, and the level of blood sugar was distinctly raised. These observations again suggested a deficiency of vitamin B. Small groups of chicks were then given relatively enormous quantities of yeast, 40 per cent of the ration. With few exceptions such chicks grew rapidly and were normal in every respect. In order to get rid of some of the extraneous material of yeast, a water extract was prepared. When this extract was fed at a level of 20 per cent of the ration, practically all the chicks grew at a normal rate, and were normal in appearance.

The potency of this extract was tested on rats, and rations containing 2.9 per cent of the water extract supported for a period of 4 weeks as rapid growth as 9.0 per cent of dried yeast. This indicates that the chick requires several times as much of the active material as does the rat. We are attempting to fractionate the water extract of yeast, in an effort to obtain the active material in greater concentration.

HONEYWELL, H. E., R. ADAMS DUTCHER and J. O. ELY (STATE COLLEGE, PENNSYLVANIA). **Curative Technique in Vitamin A Studies as Influenced by Yeast from Various Sources.**

Four commercial yeast preparations, designated respectively as I, II, III and IV, were fed, in varying amounts, to rats in curative tests for vitamin A. Yeast I possessed the anti-xerophthalmic factor but there was no evidence of the presence of the growth promoting properties which are characteristic of vitamin A. Yeast II (made by the same company, two to three years later) possessed measurable amounts of the growth promoting (A) factor, but practically all of the experimental animals were afflicted with xerophthalmia.

Yeasts III and IV (manufactured by other companies) possessed no anti-xerophthalmic properties nor was there any evidence of the presence of the (vitamin A) growth factor. When two drops of butter fat were added at the end of the period, after the body stores of vitamin A were exhausted, the growth response seemed to be dependent on the kind and amount of vitamin A-free yeast used as the source of the vitamin B complex.

Subsequent studies, in which these yeasts were fed in varying amounts during *a*, the depletion period, and *b*, the curative period, have led to the following conclusions:

1. That yeast may contain vitamin A.
2. That some evidence was obtained to indicate the multiple nature of vitamin A but, owing to the exhaustion of the supply of this yeast and our inability to obtain additional samples, this phase of the work could not be continued.
3. That our inability, in the past, to obtain the proportion of xerophthalmia in our rat colony that has been reported by other workers has been explained.
4. That the quality and quantity of the vitamin B complex exerts a definite effect on growth response, even when a constant source of vitamin A (butter fat) is supplied.
5. That the quality and quantity of the vitamin B complex in the preventive and curative periods influence the growth response (when 2 drops of butter fat are added) in a manner which leads us to believe that the size of the animal, at the beginning of the curative period, is not the sole explanation.
6. That comparative quantitative determinations of Vitamin A in foods are not possible unless each new supply of yeast is tested and the technique standardized. We have obtained differences in curative response, on 2 drops of butter fat, which vary from 100 to 300 per cent, depending upon the kind and amount of yeast ingested; for example, 0.2 gram of yeast IV was superior to 0.6 gram of yeast I.

HOOKE, D. R. (BALTIMORE). Recovery from Ventricular Fibrillation—A Cinematograph Demonstration.

The film is designed to show a method of recovering the fibrillating ventricles of the dog with theoretical application to resuscitation from ventricular fibrillation in man.

The ventricles having been fibrillated by electrical stimulation ± 25 cc. per kilo of 0.5 per cent KCl in 0.5 per cent NaCl are injected into the central end of the carotid under a pressure (150 mm. Hg) sufficient to force the fluid into the coronary arteries. The ventricles come to rest. The potassium solution is followed by ± 50 cc. per kilo of 0.23 per cent CaCl_2 in 0.9 per cent NaCl with, if need be, ± 2 cc. epinephrin 1:2000. This replaces the potassium in the coronaries and after a pause, depending upon the time the heart has been in fibrillation, the heart begins to beat, respiratory activity is resumed and the eye-lid reflex returns.

Dogs have been saved by this procedure after five minutes of fibrillation and have returned to good health.

HORVATH, A. A. (PRINCETON). The Physiological Value of Soybean Products.

Since time immemorial the soybean (*Glycine hispida*) has been the most universal article in the Chinese dietary and it has also been extensively used for food in other oriental countries. This bean is remarkable for its richness in oil (av. 18 per cent), protein (av. 40 per cent), lecithin (av. 1.65 per cent), and an insignificant amount of starch. The chief protein of the soybean, *glycinin* (a globulin), is adequate for promoting normal

growth in rats and the human organism is capable of storing more soybean nitrogen than beef nitrogen. The soybean is the only seed which contains both the water-soluble and the fat-soluble vitamins. Besides it is also rich in the fertility vitamin. Soybean oil contains a high per cent of linolic and linolenic acids and is digested by man to over 95 per cent. A soybean diet results in a rise in the blood phosphorus and lipolytic activity of the blood serum. The latter is caused by the absorption of the soybean lipase from the intestines. The alkaline ash of the soybean raises the alkaline reserve of the blood.

From the soybean the oriental people prepare a milk, a curd (*tofu*), and numerous fermented foods. Soybean milk does not coagulate on boiling alone, but the addition of $MgCl_2$ and $CaSO_4$ causes a precipitate (*tofu*). *Tofu* contains around 8 per cent of protein and 3 per cent of fat and is digested to over 95 per cent. A mould, *Aspergillus oryzae*, plays a dominant rôle in the preparation of fermented soybean foods, such as *chiang*, *miso* (both in gruel form), and *soy sauce* (liquid). The *soy sauce* contains a number of ferments (an amylase, an invertase, a hexose-mono-phosphatase) and other substances stimulating the digestion of carbohydrates and proteins and the absorption of foods (as, for instance, histamine).

HUGGETT, A. ST. G. (LONDON). **The Effect of Nervous Stimuli on Foetal Apnoea.**

These experiments were performed upon foetal goats two to six weeks before full term. The mother was urethanised or decerebrated. After Caesarean section the umbilical cord and placenta were left intact. The whole mother was immersed in saline at 38°C. so that the uterus, placenta, cord and entire foetus were kept submerged at body temperature, avoiding thereby cold air stimulation of the foetus, or inspiration of air into the lungs. Induced respirations were recorded kymographically with a tracheal cannula and tambour, or with a lever attached to the thorax.

Strong afferent nerve stimulation such as rough joint manipulations or sciatic tetanisation induced respirations while the stimulus lasted. Skin incisions, exposure to room air, nerve transection (sciatic or both vagi), and decerebration at the mid brain had no effect on foetal apnoea. Cutting an afferent nerve occasionally caused a single inspiratory gasp, and decerebration sometimes produced rapid shallow respiration, lasting about a minute, followed by apnoea as before. Stimulation of the central end of the vagus during sciatic dyspnoea caused a cessation of respiratory movements. Positive and negative lung ventilation produced single inspirations, but no inspiratory or expiratory tetanus. To produce these effects with sciatic and vagus nerves required stronger stimuli with the foetus than the mother. Further, they were not due to the anaesthetic, since they were obtained equally well from the foetuses of mothers decerebrated three hours previously.

Foetal apnoea is not due to vagal or cerebral inhibitory stimuli. The respiratory centre has a high threshold value, but with strong stimuli its response is similar to that of the adult animal. The premature foetus with intact unimpeded circulation does not respond to stimuli slightly supra-minimal for the mother. There was no sign of rhythmic activity of the respiratory centre.

IRVING, LAURENCE (TORONTO). **The Source of Expired CO₂ and Site of its Retention.**

The eviscerated or overventilated cat gives off more CO₂ than that produced by its normal metabolism. Conversely, the cat breathing a high per cent CO₂ mixture gives out less. Of the extra CO₂ expired or retained only a small amount is accounted for in blood changes. Muscle CO₂ changes about as the blood CO₂, but with the larger bulk of the muscles, the amount of CO₂ lost or retained is some four times greater. Nevertheless, the sum of blood and muscle changes does not account for half of the total lost or retained CO₂. There are reasons for considering the bones as available CO₂ reservoirs, and changes observed in the bone CO₂ of eviscerated cats would account for the CO₂ lost. On account of the great CO₂ content of bones, the changes expected are very small, and increase in bone CO₂ could not be shown in bones of cats retaining CO₂. Muscle CO₂ changes with that of blood, but only the muscle and blood changes could be established. Bone CO₂ changes were not consistent enough to be accepted as final.

IRWIN, MARIAN (NEW YORK). **Control of Permeability by Multiple Partition Coefficients.**

The penetration of dyes, weak bases, weak acids, and alkaloids into the vacuoles of living cells of *Nitella* or *Valonia* behaves as if a substance were diffusing through a heterogeneous system consisting of a non-aqueous layer separating the vacuolar sap from the external solution. The rate of diffusion is largely dependent on the partition coefficients of the penetrating substance: *a*, that between the non-aqueous layer and the external solution (coefficient E), and *b*, that between the non-aqueous layer and the sap (coefficient S). The rate of penetration of a substance is most rapid when the coefficient E is high and the coefficient S is low.

On the basis of this hypothesis it is possible to explain why some of the lipid-soluble substances do not penetrate the living cells while Overton's theory (which takes account only of the coefficient E) fails to do so.

An artificial cell was constructed consisting of a non-aqueous layer between two aqueous layers (all three being mechanically stirred). One of the aqueous layers consists of the dye solution and the other consists of the sap of *Valonia* or *Nitella* to represent the interior of the vacuole. The non-aqueous layer represents the part of the protoplasm which partakes in the control of the rate of penetration. This system acts so much like the living cell that it enables us to predict roughly the rate of penetration of a great variety of substances into these living cells.

ISAACS, RAPHAEL (ANN ARBOR). **The Physiologic Histology of the Bone Marrow.**

Study of fresh marrow on a warm stage shows that the cells are capable of considerable locomotion, and are not bound down by intercellular fibrillae such as fixed sections suggest. If the slide is tilted the blood runs in the blood vessels and repeated study has shown that every cell is in contact with capillaries, with no capillary-free groups of cells. Marrow cells placed in contact with plasma or serum separate easily and the staining properties (Wright's stain) of the tissue cells change remarkably to that of blood stream cells. Myeloblasts and myelocytes then stain as

they do in blood films from chronic myelogenous leukemia. Immature erythrocytes crumple when placed suddenly in contact with plasma or serum. This suggests that the cells are not bathed in plasma or lymph and that the blood circulation in marrow is a closed system. The nature of the intercellular substance is shown by extracting marrow with physiologic salt solution. In filtered solutions the intercellular fibrillae can be made to appear by the addition of any of the fixatives used in preparing tissues for sectioning. A certain group of the intercellular tissue fibrillae are fixation artifacts, precipitated from a more or less jelly-like, protein containing solution between the cells. The thicker the "jelly" the thicker the precipitate remaining in prepared sections of tissue, and the more liquid the "jelly" the less protein per unit area and the fewer the fibrillae. With this criterion it is seen that the immature cells are imbedded in a very thick jelly while the mature cells evidently have the power of liquefying the surrounding substances and are thus in a more fluid medium before they enter the blood vessels. This is entirely confirmed by the distribution of the cells on slides in fresh marrow smears.

ISAACS, RAPHAEL (ANN ARBOR). **Certain Features of the Physiologic Histology of the Bone Marrow.** (Demonstration)

IVY, A. C., ERIC OLDBERG, H. C. LUETH and GRANT KLOSTER (CHICAGO). **Studies on a Hormone Mechanism for Gall-Bladder Contraction and Evacuation.**

In a previous article¹ it was shown that an extract of the upper intestinal mucosa free of vaso-dilatin, on intravenous injection, causes the gall-bladder to contract and evacuate. It was also found that cross-circulation experiments yielded positive results for a hormone mechanism, *i.e.*, when acid was placed in the duodenum of one animal, the gall-bladder of both animals contracted.

The active principle acts after atropine (3 mgm.), after cervical transection. Its action is abolished by deep anesthesia and low blood pressure, and we have not been able to cause the gall bladder to contract *in vitro* by applying solutions of the active principle. We have observed by direct vision, the gall-bladder *in situ* to contract on injection of the active principle. Under its influence, the gall bladder of the cat, dog and guinea pig contracts, but not the gall bladder of the rabbit. It has no effect on the gastric musculature. Its action on the intestinal musculature is variable.

We have called the active principle "cholecystokinin."

IZQUIERDO, J. JOAQUIN (MEXICO CITY). **On the Dynamic Conditions of the Isolated Frog's Heart.**

The current view that the *hypodynamic condition* of the isolated frog's heart begins immediately with the perfusion, although based on undoubted diminution of function, takes no account of these values in the intact animal. To elucidate this point, a constant rate has been counted for several minutes in the foot-web arterioles, the frogs pithed, the hearts immersed in Ringer-Locke solution and the heart rate followed throughout.

1. Within pH limits of 7.0-8.0 and independent of relatively large variations in the K-Ca balance, the rate is notably enhanced from 2 to 5 minutes after the heart is immersed in the fluid (*hyperdynamic state*).

¹ Amer. Journ. Physiol., 1928, lxxxvi, 599.

2. In hearts immersed in large volumes of Ringer's solution, in those in small but frequently changed amounts or constantly perfused, the tachycardia gradually disappears and in about $1\frac{1}{2}$ to 2 hours the heart rate becomes constant (*steady state* or, as it is the expression of a different equilibrium with the new environment, *heterodynamic state*). The heart rate is usually at a level slightly below the normal and remains constant for 3 to 4 hours.

3. Hearts immersed in only 0.1-0.5 cc. Ringer's solution—(properly buffered)—reach the steady state within 15-20 minutes.

4. When small volumes are used, changing the Ringer's solution of the same composition at intervals longer than 10 minutes produces *secondary* increases in rate which take 15-20 minutes to disappear.

5. The *hyperdynamic state* is not a temperature effect and is independent of the sympathetic stimulation caused by pithing, and of the drop of pressure in the heart cavities.

6. The period of hyperdynamism is related to changes in the membrane equilibrium in the cell surface. Its sympatheticomimetism suggests that some increase of permeability occurs during sympathetic stimulation.

7. The practical deductions are evident.

JACCARD, P. (ZURICH). **Variation du CO_2 atmosphérique au voisinage de la végétation.**

En collaboration avec R. C. Gut, ing. forestier, l'auteur a entrepris une série de recherches concernant les variations du CO_2 atmosphérique en forêt et au voisinage de la végétation (phytosphère) ainsi que la marche de la diffusion du CO_2 dans l'air. Les déterminations ont été faites au moyen d'un appareil imaginé et construit par Ch. Gut, permettant de déterminer au millionième près les variations de concentration du CO_2 dans l'air, et cela dans un temps très court (environ 10 minutes) de sorte qu'il devient possible de suivre d'heure en heure, de jour et de nuit et dans les diverses saisons au cours de la végétation, les variations du bilan du CO_2 dans la phytosphère.

Les chiffres obtenus en forêt, montrent que les variations du CO_2 résultant de l'action concomitante de l'assimilation, de la respiration des organes verts et des processus biochimiques du sol présentent des variations diurnes, nocturnes ou saisonnières souvent assez brusques et parfois considérables. Ces variations sont influencées par les conditions météorologiques et dépendent dans une certaine mesure de la nature de la végétation (plantes herbacées, essences feuillées ou résineuses, sous-bois, arbrisseaux). Plusieurs graphiques illustrent ces variations.

Pour déterminer la marche de la diffusion du CO_2 dans l'air ainsi que la rétention de ce gaz par les diverses espèces de sol, dans les conditions d'humidité variables, on s'est servi de deux cloches de verre superposées emprisonnant une colonne d'air de 25 cm. de diamètre et de 1 m. de hauteur, reposant sur une couche de sable ou de terreau. Après avoir fait circuler dans l'appareil de l'air privé de CO_2 on introduit par la partie inférieure une quantité donnée d'anhydride carbonique, puis, par des prises d'air à divers niveaux et par des analyses faites de 15 en 15 minutes, on détermine la rapidité de la diffusion du CO_2 dans la colonne d'air et sa rétention plus ou moins grande par les divers sols utilisés. Divers graphiques montrent les résultats obtenus.

JACKSON, D. E. (CINCINNATI). **Some New Apparatus. (Demonstration)**

JACOBY, MARTIN (BERLIN). **Über die parenterale Resorption von Kolloiden.**

Für die verschiedensten Probleme der Biologie ist es von Bedeutung festzustellen, unter welchen Bedingungen Kolloide als solche resorbiert und wie sie im Blut oder in den Zellen fixiert werden. Mit Hilfe von Enzymnachweismethoden gelingt es, diese Frage zu studieren, da es so möglich ist, auch minimale Mengen von Kolloiden quantitativ zu verfolgen.

Die Bedingungen können immer gleichartig gestaltet werden, indem man bei der Untersuchung stets optimales Milieu herstellt. Natürlich muss man sich vergegenwärtigen, dass die gefundenen Verhältnisse nicht ohne weiteres verallgemeinert werden dürfen, da die einzelnen Kolloide spezifische Bindungsverhältnisse haben können. Immerhin scheint es doch weitgehende Gesetzmässigkeiten zu geben. Wichtig ist es jedenfalls, dass die Kolloide sich durchaus anders verhalten als Kristalloide. Ähnlichen Gesetzen wie die Enzyme werden wohl die Toxine und Antitoxine folgen. Von Einzelheiten sei hervorgehoben, dass die intravenös eingeführten Kolloide—als Paradigma kam die Jackbean-Urease zur Untersuchung—sehr zähe im Blut festgehalten werden. Umgekehrt gehen die Kolloide bei intraperitonealer oder subkutaner Zufuhr nur sehr langsam und unvollkommen in das Blut über. Von besonderer Wichtigkeit ist es, dass dieser Uebertritt entscheidend abhängig ist von dem Milieu, aus dem die Resorption erfolgt. Insbesondere scheint die Konzentration der in der Lösung befindlichen Salze, die Qualität der Ionen und die Wasserstoff-Ionenkonzentration der Lösung von Bedeutung zu sein. Es besteht Aussicht, auf diesem Wege, nicht nur über die Resorptionsbedingungen der Kolloide, sondern auch über ihre physiologischen Bindungsverhältnisse Wichtiges zu erfahren.

JELLINEK, AUGUSTE (WIEN). **Über akustische Reflexe an labyrinthlosen Tauben.**

Es wurden an normalen Tauben Hörprüfungen mittels Dressuren und mittels Aufwecken aus der Hypnose angestellt und dabei Tongehör für mindestens zwei Oktaven und Unterscheidung bis zu einem halben Ton festgestellt.

Die Schallreaktionen von Tauben nach doppelseitiger Exstirpation des Mittelohres unterscheiden sich nicht von normalen, sind vielmehr etwas verstärkt.

Ebenso sind die Schallreaktionen nach Exstirpation beider Lagenae verstärkt.

Nach totaler Exstirpation beider Labyrinth reagierten Tauben auf den Tonbereich a2-c3 wie normale, aber auch in verstärktem Masse. Dieses Ergebnis wurde durch Zudecken der Vögel mit einem Glassturz, durch Rufen der gesamten Federn und durch Infusion von Formalin oder Kobalt in die leeren Labyrinthkapseln nicht verändert.

Die Vollständigkeit der Exstirpation wurde bisher an einem Fall histologisch nachgewiesen.

JENDRASSIK, L. (PÉCS). **Über das Zustandekommen und die Bedeutung der Potentialwirkungen.**

Untersucht man die Wirkungen submaximaler chemischer Reize (relativ kleiner Giftkonzentrationen), so findet man sie an vielen Objekten

vorübergehend. So sind die Wirkungen besonders an vegetativ inner-vierten Geweben, z. B. glatten Muskeln von beschränkter Dauer. Es ist bewiesen, dass nicht nur Zersetzung, Wegdiffundieren bzw. Bindung des wirksamen Agens ein Aufhören der Wirkung verursachen kann. Sie klingt auch trotz unveränderter Anwesenheit des Stoffes ab, und schwache bis mittelstarke Wirkungen kommen an solchen Objekten nur bei einer Änderung der Konzentration zustande (Potentialwirkungen). Eine bei der Steigerung der Konzentration auftretende Wirkung wird am besten als Augmentationswirkung, eine bei der Senkung eintretende, als Diminutionswirkung bezeichnet.

Die Potentialwirkungen sind sehr verbreitet. Es gibt fast keine Stoffe, die keine solche ausüben könnten. Es lässt sich beweisen, dass die vorübergehende Natur der Potentialwirkungen nicht durch eine Ermüdung des Erfolgsorganes, ebensowenig durch eine Kompensation der veränderten Funktion bedingt wird. Ein zeitliches Aufeinanderfolgen in der Beeinflussung der fördernden und hemmenden Einflüsse kann auch nicht als allgemeine Erklärung gelten. Die auf Straub zurückgehenden Erklärung, dass hiebei die zwischen Zelle und Aussenlösung bestehenden Konzentrationsunterschiede (bzw. deren Ausgleichsprozesse) als Reiz wirken, entspricht gut den bisher bekannten Tatsachen. Potentialwirkungen kommen auch an glatten Muskeln mit rein myogener Automatie vor (Bauer'sches Amninpräparat). Am Darm lässt es sich zeigen, dass die Wirkung einer Substanz (Adrenalin) in Gegenwart seines Antagonisten (Pilocarpin) zwar ebenso stark jedoch bedeutend flüchtiger ist. Die Potentialwirkungen können viele pharmakologische Erscheinungen und verschiedene adaptative physiologische Funktionen verständlich machen.

JENSEN, H. and K. K. CHEN (BALTIMORE). **The Chemical Study of Ch'an Su, the Dried Venom of the Chinese Toad.**

The following compounds have been isolated from Ch'an Su: 1, *cholesterol*; 2, *epinephrin*, see Journ. Biol. Chem., 1929, lxxii, 397; 3, *bufagin* M. P. 220°, which appears to be identical with the bufagin isolated by Abel and Macht from the toad *Bufo aqua*; 4, a *N-containing compound*, M. P. 200°, which by hydrolysis gives rise to bufagin, arginine and suberic acid. The latter two compounds were identified as such. It seems therefore that this compound is chemically closely related to the bufotoxin isolated by Wieland and Alles from the European toad *Bufo vulgaris*.

JENSEN, H., O. WINTERSTEINER and E. M. K. GEILING (BALTIMORE). **Further Studies on Crystalline Insulin.**

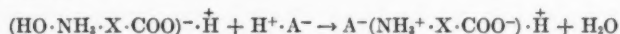
To obtain additional light on the question as to whether crystalline insulin actually is the hormone of the pancreas, we undertook to prepare insulin in crystalline form from sources other than beef pancreas which had hitherto been the only material used by us. We have succeeded in obtaining with relative ease insulin in crystalline form from the islets of certain fishes—cod and pollock. These crystals are identical in form, in physiological activity and in sulphur content with the crystals prepared from beef insulin. The physiological activity of crystalline beef insulin as compared with the international standard powder was found to be about 24 units per milligram. This value is in agreement with that re-

cently found by several other laboratories. In the crystallization of insulin from pig's pancreas we have encountered difficulties. Various reasons may account for this. The crystalline material obtained by us so far has slightly lower physiological activity and contains less sulphur than beef and fish insulin. We believe that the difference is due to impurities, which still contaminate the crystalline material and are rather difficult to remove. Further experiments are necessary before definite conclusions in regard to the properties of pig insulin can be drawn. In respect to the crystallization of insulin from commercial preparations we would like to point out that the mode of procedure in the manufacture and the degree of purity of these preparations are of importance in securing without difficulty a crystalline product.

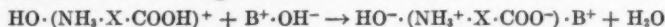
The products obtained by hydrolysis of crystalline insulin have been further studied. In addition to amino acids already reported evidence has been found for the presence of valine and of a body in the proline fraction which differs from proline. In the glycine fraction a crystalline hydrochloride was obtained apparently not identical with glycine HCl. With the relatively small quantity of insulin (2 grams) used in this experiment we did not succeed in isolating the dicarboxylic acids, glutamic, oxyglutamic and aspartic, in the fraction where they were expected. Larger quantities of material should be used before any more definite statement can be made in this regard.

JOHLIN, J. M. (NASHVILLE, TENNESSEE). The Isoelectric Point of Gelatin in Relation to Its Physical Properties.

The so-called "minimum physical properties" of gelatin (viscosity, conductivity, osmotic pressure) and its maximum turbidity are not criteria of its isoelectric point. These are properties of purified gelatin which is free from diffusible electrolytes. Pure gelatin from lime conditioned stock is a weak acid and migrates to the anode while pure gelatin from acid conditioned stock is a weak base and migrates to the cathode in an electrical field. The former can be brought to its isoelectric point by the addition of an acid and the latter by the addition of a base. There are two types of isoelectric gelatin. One is derived from gelatin from lime conditioned stock (which is a weak acid, having a pH around 5) by adding to it a stronger acid.



(X represents the gelatin radicle). The other is derived from gelatin from acid conditioned stock (which is a weak base and has a pH around 8) by the addition of a stronger base.



Either type of isoelectric gelatin is a salt of gelatin and therefore is more highly ionized than the pure gelatin from which it was derived. Such physical properties as are increased by increased ionization must therefore be greater in the case of isoelectric gelatin than in the case of pure gelatin.

JOHNS, J. P. and A. W. ROWE (BOSTON). The Influence of Pregnancy on the Visual Fields.

This study consists of a review of the literature on visual fields during the pregnant state. A series of 25 cases has been studied representing various

stages of pregnancy and study for a period of three months, postpartum. The visual field studies were made first with the Peter campimeter and second with the Ferre Rand perimeter. Radiographic examinations were made of the sella turcica both before and after parturition. A vital function survey was carried out with the cases of the series through the same period of time as the visual field studies. The employment of the Ferre Rand perimeter permitted for the first time an investigation to be conducted under standardized conditions. It insured due consideration of pre-exposure, surrounding fields, colors, distances, size of the test objects, and the fatigue elements. The study was made at an institution for unmarried mothers where daily supervision was given each case by the resident nurse under direction of the physician. The hospital administration regulated the rest periods, diet, daily activity and exercise, weight, temperature, personal hygiene and laboratory examinations. The subjects entered at any stage of pregnancy and were kept in constant residence until at least three months after delivery. This procedure gave opportunity for long continued observation of the group under definitely controlled conditions and both before and after delivery. The field studies showed a definite concentric contraction of form and color fields in the majority of cases studied and a similar incidence of blind spot enlargement was observed. The vital function studies showed only one case of definite endocrine pathology. The visual field studies in this case showed marked concentric contraction before delivery and a tendency postpartum toward return to the normal. The radiographic examination resulted in only one case of the series suggesting but not defining pathology as of the sella turcica. The measurements of this case indicated only a persistent asymmetry; the right and left side differing in their measurements. The visual fields of this case showed no pathology. The findings of these visual field studies do not show those characteristics demonstrable in the pathology of the pituitary gland where the enlargement is great enough to cause pressure and to result in bitemporal hemianopsia, superior temporal cutting, scotomata in the caeco central or para central area, or interlacing of color fields. These measurements apparently offer no objective evidence of a pituitary enlargement of sufficient magnitude to cause either pressure or contact phenomena. From the findings of the various studies made upon the series reported it seems warrantable to conclude that the field changes reported in pregnancy probably derive from functional modification rather than from enlargement or vascular changes in the pituitary gland.

JORDAN, HERMAN J. (UTRECHT). **Über die Bedeutung des "Aktivitätszustandes" für die Funktion der höchsten Zentren bei Wirbellosen.**

Die Wirkung der höchsten Centren beruht nicht nur auf einer Leitung von Impulsen, sondern auf ihrem Vermögen diese Impulse quantitativ zu beeinflussen. Sie tun dieses auf der Grundlage ihres eigenen Aktivitätszustandes. Dieser Tätigkeitszustand muss daher scharf unterschieden werden von der eigentlichen Erregungsleitung (propagated disturbance) die er nicht nur zu regeln, sondern auch zu koordinieren vermag. Als koordinierender Faktor ist es wahrscheinlich die Aufgabe des Tätigkeitszustandes bei Nerven, bei denen das "Alles-oder-Nichts-Gesetz" nicht gilt, den Erregungsablauf mit der Grösse des Reizes zu koordinieren. Bei den Schnecken ist es die Aufgabe der Ganglien, durch Anpassung ihres Tätigkeitszustandes an die jeweiligen Bedürfnisse, das periphere Reflexgesche-

hen zu regulieren. In der Regel beruht dieses Regulieren auf Verminderung der Reflexerregbarkeit durch niederen Tätigkeitszustand der Ganglien. Diese Verminderung nennen wir im Gegensatz zu echter Hemmung (z. B. Vagushemmung) "*Dämpfung*." (Das Cerebralganglion reguliert die Bewegung, die Pedalganglien den Tonus). Der Tätigkeitszustand kann experimentell beeinflusst werden: durch Cocain herabgesetzt, durch Kochsalz gesteigert. Jede Verminderung des Aktivitätszustandes dämpft dauernd das periphere Geschehen und zwar spezifisch (Cerebrale nur für die Erregung, Pedale nur für den Tonus). Reizung der Ganglien ist dagegen nicht spezifisch und gibt immer Kontraktion. Dass das Cocain nicht einen Impuls, den die Ganglien möglicherweise aussenden, wegnimmt, wird dadurch bewiesen, dass es eine normale Funktion (Dämpfung) steigert. Wegnahme der Ganglien erhöht alle periphere Tätigkeit.

Bei den Krustazeen¹ wird die antagonistische Bewegung der Beine durch erregende und hemmende Nerven geregelt. Eine dämpfende Wirkung von Seite der Ganglien war hier nicht zu erwarten; doch ergab sie sich hier, und zwar neben der Hemmung durch die Hemmungsnerven. Die Wirkung der Hemmungsnerven ist gegenüber zentralem Aktivitätszustand nicht spezifisch. Jedenfalls kann zentral durch Hemmungsnerven Erregung, durch Erregungsnerven Hemmung erzeugt werden.² Herabsetzung des Aktivitätszustandes im Scherenganglion erniedrigt die *periphere* Reizbarkeit des Schliessmuskels und seines isolierten erregenden Nerven. Diese Dämpfung ist um so wichtiger, als in der Norm das Scherenganglion den Tonus des Schliessmuskels durch den Erregernerven nur befördern kann. Auch hier wird durch das Cocain nicht ein fördernder Impuls weggenommen, denn nach Entfernung des Scherenganglions tritt die periphere Reizbarkeit wieder in vollem Umfange auf. Es handelt sich also um eine typische Dämpfung. *Wedensky*hemmung und überhaupt jede Hemmung durch Impuls kann ausgeschlossen werden. Dieser Aktivitätszustand der Zentren ist offenbar auch ein Ausdruck für zentrale Spontaneität, wie man das heute mehr und mehr auch für Säugetiere annimmt.

JOST, H. (FRANKFURT A.M.). Die Phosphatide im Stoffwechsel der Leber.

Der Fettstoffwechsel der Leber spielt sich zum grossen Teil an den Phosphatiden ab und ist mit einem beträchtlichen Phosphatumsatz verbunden. Die überlebende künstlich durchströmte Hundeleber nimmt ständig Phosphatide aus dem Blute auf und gibt anorganische Phosphorsäure ab. Diese Phosphatabgabe an das Blut ist bei der hauptsächlich auf Fettumsatz eingestellten Leber phlorrhizindiabetischer Hunde etwa 3 mal grösser als bei normalen glykogenhaltigen Lebern.

Durch Vermehrung der Phosphatide im Durchströmungsblut (durch Zusatz von Herzlecithin in feinsten Emulsion) kann die an sich geringe Acetessigsäurebildung der normalen *glykogenreichen* Leber auf das Dreifache gesteigert werden. Gleichzeitig steigt ihr O₂ Verbrauch und der R. A. sinkt ganz beträchtlich ab. Die Phosphatide wirken also als Aktivatoren der Tettverbrennung.

Bei Durchblutung der *glykogenfreien* Fettleber tritt nach Phosphatidzusatz die Bedeutung der Phosphatide für die Zuckerbildung des

¹ J. Segaar in meinem Institut.

² Die echte Hemmung beruht auf Impuls; von diesem ist die zentrale Wirkung zu unterscheiden.

kohlehydratarmen Organismus aus Fett hervor. Setzt man zu dem Zeitpunkt, in dem die spontane Zuckerbildung der Fettleber nahezu ihr Ende erreicht hat, also etwa 30 Min. nach Beginn der Durchströmung, Phosphatid dem Blute zu, so steigt der Zuckergehalt des Durchströmungsblutes kontinuierlich weiter und oft in stärkerem Masse als vorher an. Unter diesen Umständen ist eine Zuckerbildung aus den in den Phosphatiden enthaltenen Fettsäuren deutlich nachweisbar, während die entsprechenden freien Fettsäuren von der isolierten Leber zur Zuckerbildung nicht verwertet werden können.

Demnach wird zum mindesten ein grosser Teil des Fettes in der Leber erst nach vorheriger Umwandlung in Phosphatide abgebaut.

JUCCI, CARLO (SASSARI). **Esperimenti sulla Fisiologia dello Sviluppo nei Bachi da Seta. L'Eredità Materna.**

Le uova deposte da femmina di razza bivoltina di bachi da seta (*Bombyx mori*) accoppiata con maschio di razza univoltina si sviluppano, come quelle dell'incrocio reciproco, secondo il carattere della razza materna.

L'A. cerca di dimostrare che questo predominio del carattere materno-la cosiddetta eredità materna-dipende dal fatto che i fattori materni, favoriti dalla presenza di un citoplasma specificamente adatto, per quantità e per qualità, alla loro estrinsecazione, esplicano la loro attività caratteristica dominando le capacità dei fattori paterni che solo più tardi nello sviluppo riescono a farsi sentire.

Per mettere il carattere della razza paterna in condizioni di farsi sentire in tempo utile a modificare il carattere dell'uovo, l'A. cerca di indebolire il carattere materno, allevando la razza materna in condizioni sfavorevoli alla conservazione del carattere, cioè incubando il seme della razza bivoltina a temperatura piuttosto elevata, 23°C.).

Le femmine di questo lotto a 23°C e le femmine di un lotto controllo incubato a 17°C vengono accoppiate parte con maschi di Oro cinese, razza poco fortemente univoltina, e parte con maschi di Giallo europeo, razza molto fortemente univoltina.

Quanto più il carattere dello spermio è energico (razza europea) tanto più dovrebbe farsi sentire, almeno sulle uova delle femmine nelle quali il carattere allelomorfo è stato indebolito.

Così pure, accoppiando femmine bivoltine con due maschi successivamente, uno bivoltino e l'altro univoltino, oppure uno Chineso e l'altro Europeo, potrebbero ottenersi ovature miste, cioè con uova che si sviluppano ininterrottamente arrivando in pochi giorni alla schiusura, e uova che suernano in diapausa embrionale comportandosi come univoltine.

Questa sarebbe la più brillante dimostrazione dell'influenza dello spermio. Ma non si è avuta, giacché la percentuale delle ovature miste è, in questi incroci a doppio accoppiamento, altrettanto bassa come nei controlli di razza bivoltina.

Nemmeno risulta dai miei dati una differenza costante e sicura tra gli incroci con maschio oro cinese e gli incroci con maschio giallo Europeo; e neanche tra gli incroci a ♂ univoltino, considerati nel loro insieme, e controlli a ♂ bivoltino.

Sicché questi esperimenti effettuati su larga scala (parecchie migliaia di accoppiamenti) mentre confermano l'influenza potente della temperatura d'incubazione sul voltinismo, e la stretta correlazione tra capacità di sviluppo dell'uovo e tipo metabolico dell'individuo materno, non hanno

raggiunto lo scopo di dimostrare una influenza dello spermio fecondatore sulla schiusura dell'uovo.

Anzi, dopo gli accorgimenti usati per indebolire il carattere materno ed esaltare il paterno, la possibilità di una tale influenza appare improbabile. E risulta in piena evidenza la condizione di assoluta superiorità nella quale il corredo ereditario materno viene messo, in confronto al paterno dai fattori citoplasmatici.

KARRER, ENOCH and J. M. ROGOFF (CLEVELAND). A Method of Blood Transfusion by Means of Rubber Tubes Vulcanized on the Blood Vessels.

Experiments are reported in which blood transfusion was carried out on living animals by means of rubber tubing vulcanized on the vessels. The technique is described and the advantages of the method are discussed.

KATO, G., S. HARA, and S. MATSUYAMA (TOKYO). On the Point at Which the Series of the Subnormal Impulses Actually Vanish (The Studies on Wedensky Effect, Part 1).

In this series of researches a part of nerve between the stimulating electrode and the muscle was narcotised in order to study the Wedensky effect. Six kinds of experiments were made to determine the point of narcotised nerve at which the series of subnormal impulses actually vanished when "complete inhibition" was produced. We say complete inhibition only when the first normal impulse alone reaches the muscle.

1. Determination of the time of narcosis at which complete inhibition first appears in different lengths of the narcotised nerve.

2. Determination of the threshold strength inside and outside the narcotised area, first *without* and secondly *during* applications of the tetanic stimuli producing complete inhibition.

3. Determination of the point in question by means of sharply localised mechanical stimuli.

4. Examination of action currents in the narcotised area applying tetanic stimuli producing complete inhibition.

5. The sartorius muscle or M. cutaneus dorsi was divided into three parts, A, B, and C: A for stimulation, B for narcotisation and C for detection of appearance of complete inhibition. The contracting portion in B was examined under a microscope during tetanisation at A producing complete inhibition. Thickening-curve, etc.

All the experiments gave the same result; that the subnormal impulses are extinguished, not by decrement as previously supposed, but at the beginning of the narcotised area, about 3-5 mm. inside of the upper wall of the narcotising chamber.

KATO, G., M. NAKAYAMA and T. OTA (TOKYO). On the Conditions Necessary to Produce "Complete Inhibition" (The Studies on Wedensky Effect, Part 2).

The recovery curves of narcotised nerve were mapped at various stages of narcosis. As narcosis proceeds, the threshold increases enormously in the relative refractory period. Narcotising a part of the nerve between the electrode A and the muscle, the least intervals for muscular summation were determined at A (outside electrode) and at B (in the narcotised area) at various stages of narcosis. The relation between the increase of the

least intervals at both parts of the nerve and the production of complete inhibition with stimuli of various frequencies were thoroughly studied.

The following conditions are necessary:

1. A depth of narcosis in which the least interval determined at A is increased over that of B. Until this stage is reached, complete inhibition can never be produced, however frequent the stimuli might be, because the impulse is not extinguished, until this stage, in the *relative* refractory period due to the first impulse.

2. That the least interval at A is so increased that it is greater than the stimulus-interval.

3. That the stimulus-interval is smaller than the least interval at A, but greater than that at B at the moment. If the stimulus-interval is shorter than the least interval at B, then the second stimulus (impulse) vanishes in the narcotised area falling into the absolute refractory period due to the first impulse and leaves behind no "after-effect." Therefore the third may be effective. The second stimulus (impulse) is needed to fall in the relative refractory period due to the first and yet to vanish leaving an "after-effect" to inhibit the third and so on.

At the above mentioned depth of narcosis the authors demonstrated the production of complete inhibition using stimuli at regular intervals produced by a Helmholtz pendulum.

KATO, G., K. SAKAGUCHI and K. KANAI (TOKYO). **On the Inhibitory "After-Effect" Left by an Impulse Vanished in the Relative Refractory Period Due to a Preceding Impulse (The Studies on Wedensky Effect, Part 3).**

Experiments are reported in which the duration of the inhibitory "after-effect" left by the second impulse extinguished in the relative refractory period due to the first was measured with three keys of a Lucas pendulum. It was 6-16 σ . The similar experiments were made to measure the inhibitory "after-effect" left by the third (extinguished) impulse, using four keys of a Helmholtz pendulum. It was 9-20 σ .

Furthermore experiments were made in which the narcotised part was directly stimulated, during the relative refractory period, with an electric stimulus which was below the threshold at the moment. The inhibitory "after-effect" left by such an apparently ineffective stimulus was measured. It was sufficiently long (5-17 σ), in an advanced stage of narcosis, to account for the inhibitory "after-effect" left by the extinguished impulse in case of complete inhibition.

KATO, G. and T. HAYASHI (TOKYO). **The Explanation of "Paradoxes Stadium" (The Studies on Wedensky Effect, Part 4).**

It consists of two factors, namely, a frequency factor and an intensity factor.

Frequency factor. As an example let us explain one of the experimental cases. At a certain stage of narcosis a series of stimuli at a frequency of 200 per second (5.0 σ stimulus-interval) produced complete inhibition, whereas a series at a frequency of 100 per second (10.0 σ interval) produced a tetanus. At this stage of narcosis the least interval at A (outside electrode) and at B (in the narcotised area) were respectively 5.3 σ and 4.8 σ . The explanation is quite simple: the stimuli of frequency 200 pro-

duce complete inhibition, because the second stimulus (impulse) falls in the relative refractory period due to the first and leaves behind an "after-effect" which lasts long enough to inhibit the third, and in the same way the third inhibits the fourth, and so on.

Least interval at A > stimulus-interval > least interval at B. On the contrary the stimuli of frequency 100 produce a tetanus, because the second stimulus (impulse) reaches the muscle, and the third does so too, and so on.

Least intervals at A < stimulus-interval > least interval at B.

Intensity factor. It is due to the difference in the number of nerve impulses set up by the strong and the weak stimuli in question. This point was confirmed by testing the action current. Thus the intensity factor is to be attributed to the frequency factor.

KATZ, LOUIS N. (CLEVELAND). **The Calculation of the External Work of the Turtle Ventricle.**

The external work of the isolated and perfused turtle ventricle was calculated from the formula

$$W = \int_{T_0}^{T_1} PdV + \int_{T_0}^{T_1} \frac{dMv^2}{2g}$$

using a geometric construction to calculate each term on the right hand side of the equation. For this purpose, simultaneous photographic records of the intraventricular pressure and ventricular volume or the tachygram (its first differential quotient) were made by optical means; the tachygram or volume was recorded from the chamber surrounding the ventricle. The curves were calibrated in millimeters of H₂O and in cubic centimeters respectively. The work was calculated from the energy which the increments of fluid possessed at the narrow part of the hour-glass aortic cannula. The potential energy was obtained by plotting the volume against the pressure for each increment of time during ejection, then measuring the area beneath the curve with a planimeter, and converting it into gram-centimeters of work. The kinetic energy was determined in a similar manner, the volume being plotted against the square of the volume change for each increment of time during ejection. The area measured was divided by the square of the cross-sectional area of the narrow part of the aortic cannula, then by 2g, and then converted into gram-centimeters of work. These calculations were compared with those obtained by the commonly used method of calculating work, namely, taking the average pressure and velocity, and multiplying by the volume (or mass) ejected.

It was found that the usual method of averages under-estimated the potential energy by 9 per cent and the kinetic by 45 per cent on the average. The ratio of kinetic energy to total work was under-estimated by 37 per cent by the method of averages. The results obtained by the two types of calculation did not bear a constant relationship to each other, so that a percental correction of the results determined by the method of averages would not give the actual data accurately. It follows that the method of averages, commonly used to calculate the work of the heart (and its distribution), is no more than a rough approximation which may be misleading at times.

KEITH, NORMAN M., MARY WHELAN and EDWIN G. BANNICK (ROCHESTER, MINNESOTA). **The Metabolic Effect of the Administration of Nitrate.**

Studies were made of the effect of the administration of ammonium nitrate to normal subjects. Particular attention was paid to the water and acid-base balance, the urinary excretion of nitrate and other inorganic ions, and the nitrogen partition in the urine. Standard experimental conditions were secured by placing the subjects on a constant weighed diet adequate in calories, but low in salt and water content. The fluid intake was measured and constant. The experiments were divided into three periods of several days: before, during and after the injection of ammonium nitrate. The dose administered was 10 grams daily. Under these conditions there was an increase in the volume of urine, in the excretion of nitrate, chlorine and total fixed base, together with a decrease in body weight. It is believed that the latter was due chiefly to loss of water. The concentration of nitrate in blood and urine increased rapidly at the beginning of the experiment and similarly decreased rapidly after the ingestion of nitrate was discontinued. From 80 to 90 per cent of the administered nitrate was recovered in the urine. Other chemical changes were increased excretion of urea and ammonia. A disturbance in the acid-base equilibrium was indicated by an increase in the hydrogen-ion content of the urine, but was not sufficient to cause a significant reduction in the carbon dioxide combining power of the blood plasma. A similar experiment with sodium nitrate was carried out on one of the normal subjects, and 80 per cent of the nitrate was recovered in the urine. The diuretic effect was less marked. There was no disturbance in either the acid-base equilibrium or in the nitrogen metabolism. Similar studies are being carried out in cases of renal disease with edema.

KENDALL, E. C. and H. L. MASON (ROCHESTER, MINNESOTA). **A Study of Glutathione: Its Preparation, Chemical Properties, and Quantitative Determination in the Tissues.**

Forty one-hundred pound lots of baker's yeast were used for the preparation of glutathione. Modifications and changes in the method of Hopkins have resulted in increased yields and a clearer insight into the chemical reactions involved.

Reduced glutathione is best oxidized to the S-S linkage with potassium ferrieyanide. The SH group is not oxidized with quinone, but an addition product is formed. Apparently two SH groups add to one molecule of quinone. The resulting product exists in the quinone and quinol forms. Indophenols cannot be used as oxidizing agents as the same type of reaction occurs. Formaldehyde also reacts with the SH group with the formation of an addition complex, apparently analogous to the addition product between formaldehyde and HCN.

The most used method for the determination of glutathione is based on the oxidation of the SH group with iodine. In the presence of other reducing agents, the determination of glutathione by such a method gives results which are too high. A new method has been devised which is based upon the oxidation of the SH group with potassium ferrieyanide, followed by the determination of the ferrocyanide which is formed as the blue ferri-ferrocyanide salt. Folin's color reaction for the determination

of glucose has been adapted to the determination of the SH group. The total amount of ferrocyanide formed is a measure of the glutathione, only when other reducing substances are not in the solution. Formaldehyde has been shown to be a specific reagent, quantitatively preventing the oxidation of the SH group with ferricyanide and apparently not interfering with the oxidation of other reducing substances. The difference between the amounts of ferrocyanide formed before and after the addition of formaldehyde to a tungstic acid filtrate of tissues or blood is a quantitative measure of the concentration of glutathione in the reduced form. The total amount of glutathione is determined by a modification of the method of Folin and Looney, and that of Hunter and Eagles, and is based on the color produced by the reduction of phosphotungstic acid before and after the addition of a few hundredths of a milligram of a copper salt. In the presence of traces of copper, glutathione fails to reduce the reagent, although the determination of uric acid and other reducing substances is not affected. By these two methods, it has been shown that the results which have been published concerning the concentration of glutathione in the tissues are incorrect. The influence of diet, changes in basal metabolism, and other variables on the concentration of both reduced and oxidized forms of glutathione will be reported.

Hopkin's method for the isolation of glutathione has been modified as follows: The cold aqueous suspension of baker's yeast cells is treated with benzene. All the glutathione is liberated and passes into the solution. The cells are removed and the glutathione precipitated with lead acetate at a pH of 5.5. This is decomposed with sulfuric acid: the treatment with uranium acetate is omitted. The solution is treated with phosphotungstic acid at 0°C. The glutathione in the almost colorless filtrate is precipitated with mercury sulfate, which is decomposed with hydrogen sulfide. The precipitation with mercury is repeated. The final solution, which is colorless, is evaporated to a very small volume and is allowed to stand: the solution sets to a mass of crystals. These crystals have been analyzed and shown to be glutamyl-glycine-cysteine. The glycine is combined to the glutamic acid through the nitrogen of the glycine. The yield of the tri-peptide from 100 lbs. of yeast averages between 15 and 20 grams of crystals. About an equal amount of material may be secured from the mother liquor of the crystals by the addition of absolute alcohol. The fraction precipitated by alcohol has practically the same composition as the crystals. The chemical and physical properties of the crystals will be described.

KING, C. E. (NASHVILLE, TENNESSEE). **Inspiratory Irradiation.** (Cinematograph demonstration)

KLEINER, ISRAEL S. and MARION BELL (NEW YORK and COLD SPRING HARBOR). **Further Experiments on the Rate of Dialysis of Blood-Sugar in Diabetes.**

Some years ago one of us (K)¹ compared the rate of dialysis of the blood-sugar of diabetic dogs' blood with that of glucose, which had been added to normal dogs' blood. The diabetic blood-sugar dialyzed at an irregular rate, with a delayed or completely interrupted dialysis during one or more

¹ Journ. Biol. Chem., 1918, xxxiv, 471.

periods, usually the second hour. The control dialysis was not interrupted or delayed in this manner. This was interpreted as possible evidence for the existence of "combined" sugar in diabetic blood.

The present experiments extend the former work in several directions.

1. The experiments were repeated with human diabetic blood. These dialysis curves show notable irregularities, differing somewhat from those of diabetic dogs' blood-sugar, but—as in the case of the dog—showing a considerable variation from the control, consisting of normal human blood with added glucose.

2. Insulin, when added to diabetic blood, has no constant influence on the rate of dialysis of diabetic blood-sugar.

3. When diabetic blood is subjected to only a brief period of dialysis, and is then kept at room temperature without further dialysis, the blood-sugar fluctuates markedly, in some cases rising above its original value.

KLEITMAN, NATHANIEL (CHICAGO). The Onset of Sleep during Morphine Conditioned Salivation.

Dogs, in whom conditioned salivation had been developed by daily injections of morphine, are, as a rule, wide awake or in a state of excitement while they are in the stand prior to the injection of the drug. One dog (out of more than twenty) was consistently apathetic under these conditions and would fall asleep when allowed to do so. The secretion of saliva gradually decreased during drowsiness and completely stopped with the onset of sleep. Sleep apparently abolished the conditioned nausea, of which salivation is a component, for when the dog was aroused from her slumber, or if she were not permitted to sleep, the salivary secretion continued at the usual rate. This fact is in direct contradiction to the theory of Pavlov which postulates first an inhibition of the conditioned response, and then sleep as a result of the spreading of this inhibition through the entire cortex.

Light upon this phenomenon is thrown by the fact that the injection of morphine produced only a short lasting depression in this dog. Unlike other dogs she ate heartily after receiving 30 mgm. morphine subcutaneously. Also when she was left in the stand after the injection of morphine she showed gradual recovery from the depressive action of the drug by *resuming* the conditioned salivation and continuing it for hours undiminished—as long as she was kept awake. By alternately arousing her and permitting her to sleep, the conditioned salivation could be started and stopped at will.

KLISIECKI, A. (Lwów). The Linear Velocity of Blood in Arteries.

The method of measurement of the blood stream after Cybulski, improved in some details, presents the following view of blood movement.

In the abdominal aorta of a dog the velocity of blood in the diastole amounts to 500 mm. per second (250-640), in the systole it undergoes an acceleration of 45 mm. per second (9-130), and at the time of the dicrotic wave of pulse-pressure it becomes 70 mm. per second quicker than in diastole. Hence through the cross-section of the abdominal aorta there flows in the dicrotic period in 24 hours 10-120 litres more of blood than in the systolic period. If for any reason the pulsation of the aorta and other big arteries is getting worse, the dicrotic acceleration is also smaller and the heart is much more burdened in supplying the tissues with any required

amounts of blood. The dicrotic acceleration as well as the dicrotic wave of pulse-pressure is one of the characteristic signs of the movement of liquids in elastic tubes. The dicrotic acceleration protracting the influx of the liquid, contributes to the uniform outflow. The dicrotic acceleration and dicrotic wave of pulse-pressure are present, of course, also in a rubber-tube in suitable conditions.

Besides these heart waves (first-order waves) there exist in the aorta respiratory waves (second-order), which cause an oscillation of 50 mm. per second. They are synchronous with those of blood-pressure respiratory waves. Also the third-order waves are present in the motion of blood, containing 3-9 respiratory waves. They change the movement periodically to 100 mm. per second.

In the femoral and carotid artery of a dog the velocity is 600 mm. per second (509-664), the systolic acceleration 50, the dicrotic acceleration 55-60, but often the latter does not exceed the former or is smaller. The respiratory waves are changing the movement for 20-70, and the third-order waves for 100 mm. per second.

In the lower part of the femoral artery the velocity is 450 mm. per second (270-500), like that in the aorta, the systolic acceleration is 48; the dicrotic acceleration is here rarely greater than the systolic (10 mm.), usually smaller. The respiratory changes of the blood movement are 50 mm. per second (10-45) and third-order waves 30 mm. per second.

In the arteria saphena (a ramus of the femoral artery) of 0.5-1.2 mm. bore, the velocity amounts to 250 mm. per second (107-410), the systolic acceleration 24 mm. per second (3-70) and the dicrotic acceleration in the vessels of these diameters never surpasses the systolic. The respiratory waves in the arteria saphena are of 20 mm. per second (10-45) and third-order waves 30-70 mm. per second.

In the ramus plantaris arteriae saphenae of 0.38-0.2 mm. bore, the velocity is 135 mm. per second (48-270), if this vessel possesses a greater diameter (0.85 mm.) the movement is quicker (407 mm. per second). The systolic acceleration is here very small (0.5-3 mm.), and the blood-stream is often uniform as in capillaries. The respiratory waves in this artery are 4-7 mm. per second; the third-order waves could not be observed there.

With regard to the relationship of the blood movement in some arteries simultaneously registered, we meet with the interesting fact that in an artery the velocity as well as the systolic acceleration are smaller than in its ramus (*e.g.*, in the femoral artery the velocity is 270 mm. per second, the systolic acceleration 38 mm. per second and in the a. saphena the velocity is 300 mm. per second and the systolic acceleration 70 mm. per second. Also in the aorta the velocity is smaller than in femoral or carotid artery, according to the hypothesis of R. Thomé. But this fact depends evidently not only on the smaller sum of the cross-sections of the branches of the aorta, because the same relationship is to be seen in quite peripheral rami, the sum of the cross-sections of which is much greater than that of their arteries. Such a relationship of the movement in various arteries is due to the pulsation of arteries.

KLISIECKI, A. (Lwów). The Relation of Movement Oscillation to Blood-Pressure Waves.

The experiments in which I investigated blood movement simultaneously with blood-pressure in the same vessel (by the help of a glass-tube con-

nected with two right-angle cannulas, filled up by Ringer's fluid to some level and closed in their upper end) show that there exists a complete harmony between velocity and pressure.

In the heart's waves the systolic acceleration appears at the same moment as the systolic pressure, the diastolic velocity comes in view simultaneously with diastolic pressure. As to the size of pressure and velocity, they are both in some certain constant proportion, which is disturbed by respiratory waves or by changes of the ebb through the action of precapillaries.

The dirotic acceleration is also concordant with the dirotic pressure in small arteries. But in big vessels there is a disharmony, because in the aorta during the dirotic pressure the blood movement is more accelerated than during the systolic pressure; in the upper part of the femoral and carotid arteries the dirotic acceleration is mostly equal to the systolic one or a little smaller; in the lower part of the femoral artery the diastolic acceleration exceeds the systolic on the top of the respiratory waves, if the respiration is sufficiently deep. But this disharmony proves neither the existence of reflected waves nor their influence upon the blood motion, because after the systolic acceleration the blood movement does not show such a relaxation as in the former experiments of Lortet and in recent investigations of Ph. Broemser, but on the contrary it is quicker.

The respiratory waves of velocity and pressure show a general parallelism. The maximum of the systolic pressure of a respiratory wave synchronises in any given heart-period with the maximum of the dirotic acceleration and with that of diastolic velocity; only in the next heart-period the maximum of diastolic pressure of this respiratory wave coincides with the maximum of the systolic acceleration. This proves that the rising pressure of the respiratory waves extending over the whole pulsating system diminishes the resistance and so facilitates the blood flow; since the peak of the pressure wave reaches each respective artery more quickly than does the maximum movement produced by the heart, therefore the maximum of systolic respiratory pressure causes at first the maximum of the dirotic acceleration and of diastolic velocity. The same is caused by systolic pressure in the heart beat, large portions of the arteries being extended, and that is why after each systole, *i.e.*, during the dirotic and diastolic times, blood flow is facilitated. But this influence of the systolic pressure on the flow in short first-order waves is rather difficult to see by this simple method, but it is manifest in long respiratory waves which, from this point of view, could be regarded as long heart waves. The respiration plays a very important part also in the flow of arterial blood.

The relationship of third-order linear waves to those of pressure has not yet been investigated.

KLISIECKI, A. (Lwów). The Blood-Pressure in Pulsating Arteries.

The measurement of pressure by the help of the air-manometer explains also the question of blood-pressure. The rule is that the amplitude of pressure-waves in the arterial branches is smaller than that in main arteries and lies in the sphere of central amplitude; the diastolic pressure rises towards the periphery more and more, the systolic pressure diminishes, and in small arteries below 0.3-0.2 mm. bore, all waves of pressure as well as of movement are extinguished. But it may occur that the systolic pressure in a ramus is higher than in the artery at a given time or, that the diastolic

pressure is lower in a peripheral artery; but it is not an habitual state, because in the same experiment the diastolic and systolic pressures, especially in smaller arteries, rise or fall relatively to the action of precapillaries. The scheme of blood-pressure is shown by the heavy lines in Figure 4; the fine lines represent the pressure in some experiments of mine. In this way the blood-pressure in small vessels is levelled, and a great part of the heart's energy, which is not taking part in the blood-movement before it is transported to the capillary system, is at the disposal of the blood-flow in the tissues.

In the course of the arterial-blood three segments can be discerned. All the pulsating arteries represent a cistern (reservoir), at the end of which the blood-pressure is high and steady; from it the blood flows out through the non-pulsating, tonic contracted channels just as the water in an irri-

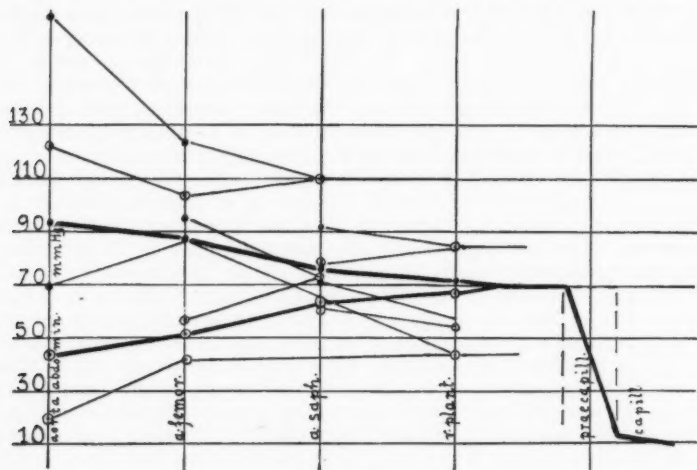


Fig. 4

gation-system runs through the sluices in a dam. This is the second segment. The third is represented by the irrigating-channels, the capillaries. In the first segment there is a high blood-pressure, in the third segment it is one tenth as high. The pressure in the second segment depends on the contraction or dilatation of the respective vessel; if there is a contraction before the capillaries the pressure is high, if on the contrary the non-pulsating vessel is dilated there is apparent a lower pressure than in the pulsating system. From this point of view a difference of pressure in a big and a small artery can not be regarded as an argument for the regular arterial pressure fall, because the pressure in peripheral vessels is changing. This is concordant with the statement of Th. Joung and Poisseuille.

The behaviour of blood-flow and pressure in the arteries is characterised by particular signs, such as dicrotic acceleration of the movement, the smaller linear velocity and smaller systolic acceleration of the blood in the

arteries than in their rami, as well as by quicker linear movement in the peripheral vessels not proportional to the sum of their cross-sections; farther the lack of pressure-fall in the pulsating vessels, the lower systolic pressure in the arteries (*e.g.*, femoral, carotid artery) than in their rami, which sometimes occurs. We have no proofs for the influence of the reflexion of the heart's wave in the periphery as the cause of these characteristic signs. The only reason is the pulsation of arteries. In fact we find the same phenomena of movement and pressure in a ramified system of rubber-tubes, when their pulsation is distinct and strong.

KLOSTER, GRANT, A. C. IVY and H. C. LUETH (CHICAGO). **The Preparation of Solutions Containing "Cholecystokinin."**

We have used the first six feet of the intestine of dogs, hogs, sheep, and cattle. The most highly purified solutions have been prepared from the dog's intestine. We have not been able to extract the active principle from the gastric mucosa, the liver, the spleen and the kidneys.

The freshly excised loop of duodenum and jejunum is washed with cold water and then filled with 0.4 per cent HCl, or 0.5 per cent H₂SO₄. After one-half hour the acid is removed from the loop and filtered. The activity can then be precipitated from the filtrate with 5 per cent trichloroacetic acid or by saturation with sodium chloride. The latter is preferred since it yields a product which can be kept indefinitely and is usually quite free of vaso-dilatin.

The sodium chloride precipitate has been handled in a number of different ways. A uniform product can be obtained as follows: The NaCl precipitate is extracted with 95 per cent ethyl alcohol. Much of the secretin and any remaining dilatin passes into the alcohol, but the cholecystokinin is insoluble. The 95 per cent alcohol insoluble residue is taken up in water. We call this S. III. To this solution is added NaOH until the pH is 5.0-5.5. A precipitate results which is filtered off, the activity being in the filtrate. The filtrate is then precipitated with 5 per cent trichloroacetic acid. The precipitate which contains the activity is dissolved in hot water (we call this 1802) and filtered. The procedure down to this point has never failed in our hands and has been tried at least fifty times. On boiling this solution (1802) with a "bumping stone" for about twenty minutes and then cooling, a precipitate forms which can be filtered off, the activity remaining in the filtrate. We call this 1802 Coag. On evaporating this to dryness at a low temperature (55°C.) and then redissolving in water, we have obtained a gall-bladder contraction with 2.8 mgm. of solid material. The evaporated residue instead of being redissolved in water can be washed with ether and acetone and then extracted with 80 per cent alcohol. The 80 per cent alcohol extracts all the secretin and usually most of the "cholecystokinin." On evaporating the 80 per cent alcohol and taking up the residue in water, we have obtained secretin in a dosage of 0.2 mgm. (solids) and "cholecystokinin" in a dosage of 2.2 mgm. (solids). These two latter procedures do not yield uniform results. The purity varies and not infrequently the activity is lost.

Highly purified solutions of secretin and "cholecystokinin" with a pH of 4.5-5.0 on standing in the ice-box for from one week to two months become cloudy and inactive, but with a pH of 3.0 have been kept in the ice-box for four months. The S. III solution will keep in the ice-box more than a year, even with mold growing on it.

Bile salts only sometimes precipitate "cholecystokinin." From our studies up to the present, we believe that "cholecystokinin" is closely allied to, but not identical with, secretin.

KNOWLTON, F. P. and C. J. CAMPBELL (SYRACUSE, NEW YORK). **An Electron-Tube Stimulating Device. (Demonstration)**

KNUDSON, ARTHUR and PHILIP J. SCHAIKLE (ALBANY). **Chemical Changes in the Body Resulting from Exposure to Ultra-High Frequency Field. I. Blood Chemical Findings in the Dog. II. Acid-Base Balance in the Plasma of Dogs.**

During the operation of a short-wave radio transmitter, striking heating effects in the vicinity of the antenna have been noted.¹ The general effect on animals when placed in the field of short radio waves of from 25,000 to 10,000 kilocycles (12-30 meters) is a marked heat production so that the body temperature is raised considerably in a short period of time. The rectal temperatures of dogs have been raised to 105-110°F. (40.5-43°C.) and maintained at these fever temperatures for varying periods of time. With extreme temperatures of 108-110°F. maintained for a period of 30 to 60 minutes very marked changes in the blood are brought about. A marked decrease in blood volume occurs, with a coincident increase of cell volume.

There is a great increase of non-protein nitrogen and lactic acid. Sugar shows at first an increase but in those experiments where heating is continued over a long period the sugar is normal or even below the normal level. The alkaline reserve and the pH are greatly reduced indicating a condition toward acidosis.

A study was also made of the serum electrolytes such as the total base, chlorides, bicarbonate, protein, lactic acid, and inorganic phosphates. The level of total base, protein and chlorides tend to remain normal but in extreme treatment these increase though the increase does not seem to be out of proportion to the changes of the blood volume. The lactic acid is greatly increased and the bicarbonate markedly reduced.

KOCH, E. (KÖLN). **Weitere Untersuchungen über die Blutdruckzügler.**

Als *Blutdruckzügler* bezeichnet H. E. Hering die beiden Nervenpaare, deren Rezeptoren im Aortenbogen und im Sinus caroticus liegen. Diese Stellen entsprechen ontogenetisch dem 3. und 4. primitiven Aortenbogen.

Die beiden Aorten- und die beiden Carotissinus-Nerven bilden eine funktionelle Einheit. Ihre natürliche Funktion besteht in einer Selbststeuerung des Blutdruckes, durch die sowohl Steigerungen als auch Senkungen gedämpft werden. Bei künstlicher Reizung oder Ausschaltung von Blutdruckzüglern wirken die übrigbleibenden als Antagonisten. Durch zahlenmässige Auswertung der Blutdruckanstiege, die durch nacheinander erfolgende Ausschaltung auftreten, lässt sich nachweisen, dass es ausser diesen vier Blutdruckzüglern keine weiteren mehr am Kreisläufe gibt. Nach Ausschaltung sämtlicher Blutdruckzügler bleibt der Blutdruck für immer erhöht; der Kreislauf verfügt dann über kein Mittel mehr, den Blutdruck dauernd wieder auf die normale Höhe herabzusetzen.

Durch Unterbindung sämtlicher peripher von der Carotisteilungsstelle abgehenden Gefässe kann man ein *Carotissinuspräparat* mit erhaltenem

¹ H. R. Hosmer. Science, 1928, lxxviii, 325.

Sinuskurven herstellen. An einem solchen Präparat lässt sich (ausser anderem) die Beziehung, die zwischen der Höhe des endoarteriellen Druckes und dem Ausmasse der Blutdrucksenkung besteht, quantitativ verfolgen. Die so erhaltenen Kurven entsprechen in ihrem Verlaufe den Elastizitätskurven (Kubische Erweiterung) lebender Arterien mit einem in der Mitte gelegenen Steilwendepunkte. Ihr Differentialquotient ergibt den Wirkungskoeffizienten des Sinuskurven; er hat in der Höhe des normalen Blutdruckes ein Maximum: am Kaninchen bei 90, am Hunde bei 120, an der Katze bei 145 mm Hg.

KOCH, E. (KÖLN). **Demonstration am Carotissinuspräparate. (Demonstration)**

KOCH, F. C., CARL R. MOORE and T. F. GALLAGHER (CHICAGO). **The Effects of Extracts of Testes in Correcting the Castrate Condition in the Fowl and in Mammals.**

Properly prepared lipid extract from bull testicles when administered by subcutaneous or intramuscular injection in the brown leghorn capon causes a remarkable growth of comb, ear lobes and wattles. This reaction is a semi-quantitative one. A similar extract when injected into the castrated rat prevents or corrects the atrophy of the seminal vesicles as well as the degenerative changes in the anterior lobe of the prostate. In the pre-puberally castrated rat the injection of the extract brings about the growth of an histologically normal prostate. In the guinea pig several castration effects can be overcome by the injection of this extract. The loss of sperm motility in the epididymis can be corrected by injections to the same extent as by a cryptorchid testis. The loss of sperm in a castrated guinea pig as measured by the ejaculation test can be in part corrected and rebuilt by the injection of this extract. The atrophy of the seminal vesicles is also retarded or inhibited by these injections.

KOEHLER, ALFRED E. and LILLIAN EICHELBERGER (CHICAGO). **The Separation of a New Physiologically Active Principle of the Suprarenal Gland.**

An epinephrin-free substance has been separated from the suprarenal gland that is capable of elevating the basal metabolic rate and producing improvement in various types of clinical asthenias.

The calorogenic activity of this substance administered to animals has proved of great value in its separation and assay.

Its preparation depends upon the separation of epinephrin and other interfering substances such as choline, its activation and finally concentration by the removal of inactive substances. Each of these processes may be accomplished in various ways. Two processes will be described, one depending upon the active principle being carried down with the protein precipitation and the other by its extraction with the lipid fraction.

Protein precipitation. The aqueous extract of the fresh glands is adjusted to pH 4-5, preferably 4.8, with acetic or other non-oxidizing acid and the protein precipitated by three-fourths saturation with NaCl or $(\text{NH}_4)_2\text{SO}_4$. This precipitate can then be washed free from the uncombined epinephrin. Such a precipitate, or its aqueous or acid extracts, however, have a depressing effect on the basal metabolism and unfavorable

clinical actions. If this precipitate is protected from oxygen, the depressing action will disappear on standing and it will acquire the property of raising the metabolic rate. This change can best be accomplished by heating the precipitate with 2 to 3 M HCl on the boiling water bath for ten to fifteen minutes. The active principle can then be separated from the bulk of the protein mass by drying the acid solution *in vacuo* so as to remove all moisture, extracting with absolute methyl alcohol, adjusted to pH 4.5 with ammonia in absolute methyl alcohol (pH measured by transferring small amounts of alcohol mixture to aqueous system) and precipitating with 7 volumes of acetone. Further purification can be effected by redissolving in alcohol and precipitating with acetone.

Lipoid extraction. The fresh ground glands are extracted with methyl alcohol-ether mixtures, starting with 80 per cent alcohol and 20 per cent ether and gradually reversing this ratio on subsequent extractions. The alcohol and ether are then distilled off *in vacuo* and the water-lipoid residue extracted with ether. The separated ether extract is washed with water, dried over anhydrous Na_2SO_4 and the ether evaporated. The residue is then treated with absolute methyl alcohol containing dry HCl gas and heated on the water bath for fifteen minutes. The reaction of the alcohol solution is then adjusted, precipitated with acetone as in the protein precipitation method and similarly purified. Evidence to date indicates that the physiological effect of the substances prepared by these two methods is similar.

KOEHLER, ALFRED E. and A. BAIRD HASTINGS (CHICAGO). **Metabolic Studies Following the Administration of Suprarenal Extracts.**

It was found that extracts, free from adrenalin, prepared from the suprarenal gland raised the metabolism of dogs and mice when administered orally. The calorogenic effect on human subjects with a low metabolic rate is marked. These subjects exhibit a low mechanical efficiency which is raised to approximately normal by the extract. An attempt has been made to determine what factors are concerned in the alteration in metabolism. The evidence to date indicates that carbohydrates are utilized more efficiently and proteins are spared.

A study has also been made of the oxygen consumption, CO_2 production, and lactic acid formation by tissues excised from animals whose metabolism has been altered by various extracts.

KOMM, ERNST (DRESDEN). **Über die Dielektrizitätskonstante biologischer Stoffe (zugleich Beschreibung einer Methode zur Bestimmung dieser Konstante).**

KOPPÁNYI, THEODORE (SYRACUSE). **Respiratory Adaptations in Diving Animals.**

Diving animals in general are capable of holding their breath for a long time (10-20 minutes) while under water. The afferent nerve endings of the reflex arc controlling this phenomenon are in the nostrils, since pouring water over the nostrils induces apnea in the duck and also in the muskrat.

Besides this "submergence apnea" there is another respiratory adaptation in diving birds and the muskrat, an apnea resulting from certain peculiar positions of the animal's head and neck in space. This "postural

apnea" is best elicited upon straightening the neck or dorsiflecting the head upon the neck while the animal is lying on its back. During postural apnea respiration occasionally breaks through, but cases of complete apnea of 10 minutes' duration have also been observed in the duck. It is actually possible to kill the duck by maintaining this postural apnea until the animal dies from lack of oxygen.

It is indeed a remarkable fact that inhibitory nervous influences can counteract the chemical stimulation of the respiratory center by the accumulated CO_2 in the blood. It has been suggested that in these cases CO_2 might act not as a respiratory stimulant but rather as a depressant. It was shown, however, that CO_2 in diving birds and mammals is a stimulant to the respiratory center and depresses respiration only in high concentrations. Acting as an irritant on the upper respiratory tract in higher concentrations it inhibits respiration.

Submergence and postural apnea are accompanied by a marked slowing of the heart and a rise in blood pressure. Both of these phenomena are due to the CO_2 stimulation of the vaso-constrictor and cardio-inhibitory centers.

Pharmacological studies of these apneas revealed the fact that respiratory stimulants like caffeine, ammonium chloride, et cetera, do not interfere with and do not interrupt postural apnea. Respiratory depressants like morphine, however, enhance postural apnea.

KOTSOVSKY, D. (CHISINAU). **The Origin of Senility.**

Die Ernährungsfunktion. Die Bedingungen für den Stoffwechsel in den verschiedenen Teilen der Zelle, soweit sie sich dem Abhängigkeitsgesetz der inneren von den äusseren Speise aufnehmenden Teilen unterordnen, sind bei einfachen und differenzierten Zellen verschieden, um so mehr aber bei einfachen und differenzierten Organismen. Bei ersteren werden die toxischen Produkte des Stoffwechsels zwischen Zelle und Medium leicht entfernt, bei den zweiten ist die Ausscheidung erschwert, deshalb ungenügend.

Die Funktion des Wechselstandes zwischen Ruhe und Tätigkeit. Dank dieser Eigenschaft der Ernährungsbedingungen fehlt bei den einfachsten Organismen die Notwendigkeit eines längeren Ruhezustandes zur Entfernung schädlicher Produkte der Lebenstätigkeit und zur Anhäufung potentieller Energie in der Bioplastik und den mit ihr verbundenen Schutzfunktionen.

Die Funktion des Lebensschutzes, ausgedrückt durch eine Reihe von Schutzreaktionen der Zelle oder ganzer Zellenkomplexe auf Erregungen, die eine Störung ihres biologischen Gleichgewichtes hervorrufen, verändern bei fortschreitender Evolution des Tierreiches ihren Charakter im Sinne einer Progression ihrer Unzulänglichkeit für den Lebensschutz. Der Wechselstand zwischen Ruhe und Tätigkeit, als eine der Funktionen des Lebensschutzes, ist bei niederen Tieren nicht hinreichend scharf ausgedrückt, während bei höheren Tieren diese Periode deutlich umgrenzt erscheint (Schlaf-funktion).

Die Funktion des Wachstums und der Regeneration. Der Prozess des Schlafes als hauptsächlichste Schutzfunktion des Körpers gegen die im Wachzustand gebildeten schädlichen Erzeugnisse der eigenen Lebenstätigkeit, steht in Verbindung mit dem Prozess des Wachstums; die Wach-

tumskurve geht parallel mit der Kurve des nachlassenden Schlafbedürfnisses.

Die Funktion der Vererbung. Der Wachstumsprozess ist eng mit dem durch ihn bedingten Verfall der Zelle verbunden und beide Vorgänge ordnen sich den Gesetzen der Vererbung unter. Die Vererbung wirkt bei Evolution der genannten Funktionen verändernd auf den Mechanismus des Alterns ein, das bei den einfachsten sich auf primitive Weise ernährenden Organismen gänzlich fehlt, und folglich verändert sie auch die ursprüngliche Intensität der Schutzfunktionen (Entfernung toxischer Stoffwechsel-Produkte, Fehlen einer längeren Schlafnotwendigkeit und starke Neigung zur Regeneration).

Die Entstehung des Alters. Da die Schutzfunktion bei höheren Tieren eine komplizierte Form annimmt, wie z. B. bei den Erscheinungen der Immunität, Anaphylaxie und Allergie, so muss der Entstehung des Alters eine weit umfassende Erklärung gegeben werden, und zwar vom Standpunkte der im tierischen Organismus mit der Differenzierung fortschreitenden Schwächung der Immunität gegen schädliche Produkte der eigenen Lebenstätigkeit, die sich progressiv anhäufen und das biologische Gleichgewicht der Zellenkomplexe stören.

Das Problem der Altersbekämpfung besteht, von Obigem ausgehend, in der Verstärkung aller Gewebe und Organe und insbesondere solcher Gewebe, die eine feinere differenzierte Struktur haben, wie die Gewebe des Zentral-Nervensystems.

Diese Gewebe haben die allerungünstigsten Ernährungsbedingungen, werden bei unzulänglichem Schlaf vor allem zuerst betroffen, halten am frühesten von allen im Wachstum inne, sind am wenigsten zur Regeneration geneigt und deshalb werden an ihnen am ehesten die Alterssymptome konstatiert.

KREBS, H. A. (BERLIN). **Manometrische Messung der Peptidspaltung.**

Peptide sind stärkere Säuren als die Aminosäuren aus denen sie aufgebaut sind. Daher werden Peptidlösungen bei der Spaltung der Peptide alkalischer, und löst man Peptide in Ringerlösungen von physiologischen Bikarbonat- und Kohlensäuregehalt auf, so absorbiert die Lösung bei der Spaltung der Peptide Kohlensäure. Die Absorption der Kohlensäure wird manometrisch nach Warburg gemessen. Die gespaltene Peptidmenge wird an der Kohlensäureabsorption berechnet. (Siehe Biochem. Zeitschr., 1929, cex, 7.)

KŘÍŽENECKÝ, JAROSLAV (COLD SPRING HARBOR, L. I.). **Thymus Antagonism to the Action of the Thyroid in Reducing Body Weight.**

Previous experiments in pigeons showed that the decrease of body weight produced by dry thyroid substance administered *per os* can be reduced to about one-half by the simultaneous administration of dry thymus substance. This effect was interpreted as indicating hormonal antagonism of thymus against thyroid. To answer the question whether nucleic acid, rather than thymus hormone, was responsible for this antagonism the following tests have now been made on ring doves (5 per group dosed daily):

Control group: 0.3 gram peptone in glycerin emulsion.

Thyroid group I: 0.1 gram thyroid + 0.2 gram peptone in glycerin emulsion.

Thyroid group II: 0.2 gram thyroid in gelatin capsules.

Thymus group: 0.2 gram thymus + 0.1 gram peptone in glycerin emulsion.

Thymus + thyroid group I: 0.1 gram thyroid + 0.2 gram thymus in glycerin emulsion.

Thymus + thyroid group II: 0.2 gram thyroid + 0.4 gram thymus in gelatin capsules.

Nucleic acid group: 0.015 gram nucleic acid (obtained from spleen) + 0.3 gram peptone in glycerin emulsion.

Thyroid + nucleic acid group: 0.015 gram nucleic acid + 0.1 gram thyroid + 0.2 gram peptone in glycerin emulsion.

Experiments done in February and March; duration 34 days.

Results (decrease in all): In control group an average decrease in body weight of 4 per cent. In thyroid group I, of 19 per cent. In thyroid group II, of 22 per cent. In thymus group, of 6 per cent. In thyroid + thymus group I, of 12 per cent. In thyroid + thymus group II, of 10 per cent. In nucleic acid group, of 10 per cent. In thyroid + nucleic acid group, a decrease of 27 per cent.

KROGH, AUGUST (COPENHAGEN). The Utilization of Dissolved Organic Substances by Aquatic Animals.

The absorption of dissolved organic substances is studied in experiments of short duration in which the animals to be studied are enclosed in suitable vessels perfused with artificial solutions or natural water. In the ingoing and outgoing water determinations are made of dissolved oxygen and organic substances generally as well as the specific substance under investigation. When the absorption of a substance is studied in relation to the oxygen intake its possible significance for the total metabolism becomes at once apparent.

The determination of dissolved organic substances is performed as follows:

A few milligrams of organic substances are burned in pure nitrogen by means of cupric oxide. The combustion tube is intercalated in a gas analysis apparatus between two gas burettes and after the main combustion a measured volume of oxygen is taken through the tube at a red heat. This finishes the combustion and oxidizes the copper formed back into cupric oxide. The analysis of the gas mixture gives the CO_2 formed, the nitrogen liberated and the oxygen used in the combustion. It is possible therefore to calculate the heat of combustion and to distinguish roughly between nutritive substances and waste products.

When solutions like natural water containing some mgm. per l. are to be determined they are first concentrated in a vacuum. Calcium and magnesium which interfere with the combustion are removed and the concentrated solution is slowly introduced into the combustion tube and here evaporated to dryness in a vacuum. Even large quantities of alkali chloride do not interfere with the combustion.

So far I have found that glucose can be taken up by mussels from solutions containing 20 mgm. per l. in quantities corresponding to $\frac{1}{4}$ of the respiratory exchange. In the other animals studied (*Daphnia*, fishes and tadpoles) the absorption is too slight to be definitely established and is insignificant from the point of view of the economy of the organism.

A green alga (*Scenedesmus*) growing in a solution of suitable salts does give off organic substances to the water, but the quantities are very small compared with those present in the organism.

KROGH, AUGUST (COPENHAGEN). **Determination of CO₂ in Fluids by Microtitration. (Demonstration)**

The apparatus is a glass bulb of about 60 cc. capacity with a tap on one side for letting in the fluid to be determined. The bulb is connected through a ground joint with a small receiver.

A little phosphoric acid is introduced into the bulb and the whole is evacuated and thereupon filled with CO₂-free air. While CO₂-free air is flowing in under a low pressure the receiver is disconnected and a suitable volume of titrated baryta is introduced by means of a syringe acting as pipette (Rehberg). The receiver is again connected with the bulb and the whole evacuated before the introduction of the fluid to be determined.

The CO₂ is driven over into the receiver with the water vapour liberated by gentle heating, the process requiring only 3 minutes. Finally the apparatus is again filled with CO₂ free air; the receiver is disconnected and the baryta titrated with hydrochloric acid from a microburette. The accuracy obtainable is from $\frac{1}{2}$ to $\frac{1}{3}$ cmm. of CO₂.

KRUMBHAAR, E. B., E. WILSON and R. W. GARLICH (PHILADELPHIA). **The Relation of the Normal Adult Mammalian Spleen to Red Blood Cell Formation.**

An inhibitory effect on the production of red cells has been attributed to the spleen, chiefly on account of the relief of anemia that often follows splenectomy clinically; and secondly, the transient polycythemia that sometimes follows removal of the normal spleen (post-operative anhydremia?).

Evidence is presented to show that the spleen normally has the opposite (*i.e.*, favorable) effect on blood cell production. Splenectomy in normal mammals under standard conditions is followed by an anemia that varies in duration and severity approximately with the spleen-body weight ratio of a given species. The anemia can be modified by an iron rich diet. The increased loss of iron that sometimes follows splenectomy appears to be a factor in this anemia.

A slight increase in erythrocyte concentration and reticulocyte percentage may be found for 1 or 2 days after splenectomy. It is not clear whether this is due to increased erythropoiesis or to anhydremia and change in speed of maturation of the erythrocytes.

Parenterally introduced splenic extract has a greater effect in increasing the peripheral red cell count than have similar extracts of other organs.

The delayed regeneration from hemorrhagic anemia that was found by Honda when spleen or bone marrow is fed to rabbits was not observed by us, when the conditions of his experiment were duplicated as far as possible we found no demonstrable effect—favorable or unfavorable—and suggest that, if present, it might be explained rather through the inhibiting effect of animal food on the appetite of an herbivorous animal than through any specific anti-hemopoietic effect of the spleen.

KUNDE, M. M. (CHICAGO). **The Basal Metabolic Rate in Experimental Cretinism and Myxedema. Studies on Metabolism VII.**

The basal metabolic rate of dogs thyroparathyroidectomized in the

puppy or adult stage is lower than that of normal dogs only in those animals showing other symptoms of thyroid deficiency. Incomplete control of the parathyroid tetany masks all effects of the thyroid deficiency on the basal metabolism.

LA BARRE, JEAN et PIERRE DESTREE (BRUXELLES). **Influence de l'hyperglycémie et de l'hypoglycémie des centres nerveux supérieurs sur la sécrétion externe du pancréas.**

On provoque de l'hypoglycémie par l'insuline, la dècaméthylènediguanidine ou l'hépatéctomie chez un chien chloralosé A, dont la double circulation carotido-jugulaire nourrit la tête isolée d'un congénère chloralosé B, réuni à son tronc uniquement par les pneumogastriques. Les centres nerveux supérieurs de B, réagissant à cette hypoglycémie par une diminution de la sécrétion du suc pancréatique déterminée dans ce tronc par l'injection lente et continue intrasaphène de sécrétine. Quand on injecte une dose massive de glucose par voie intrasaphène chez le chien A, dont la double circulation carotido-jugulaire irrigue la tête isolée de B, les centres nerveux supérieurs répondent à l'hyperglycémie en accroissant la sécrétion du suc pancréatique dans le tronc réuni à cette tête seulement par les vagues. Si l'on sectionne une demi-heure après l'injection de glucose les pneumogastriques qui relient la tête au tronc, la quantité de suc sécrétée diminue aussitôt.

Après une phase d'hypoglycémie de la tête isolée accompagnée d'une diminution de l'excrétion pancréatique, il suffit de remonter par une injection massive de glucose la glycémie du chien nourricier A, au delà de la normale pour accroître la sécrétion du suc pancréatique du tronc de B, relié uniquement par les vagues à sa tête.

Un pancréas circulatoirement indépendant du restant de l'organisme mais laissé sous le contrôle de son système nerveux réagit encore à l'hyperglycémie des centres encéphaliques par une augmentation de la sécrétion exocrine.

Les modifications de la glycémie encéphalique retentissent donc par la voie des vagues sur la sécrétion externe du pancréas.

LAPICQUE, L. and M. LAPICQUE (PARIS). **Chronaxie of Subordination as Determined by Posture.**

In a motor nerve severed from nervous centers, there is a definite chronaxie, the one studied for years. Such a chronaxie, related to structural conditions (it is inversely proportional to the diameter of the fiber) and to the colloidal properties of the protoplasm (for instance, to the capacity for swelling in hypotonic solutions), may be called *constitutional chronaxie*.

But in a spinal motor nerve, having natural connection with centers, especially with the midbrain (for instance, in a decerebrated frog), chronaxie is variable, generally shortened with regard to its constitutional value. This last will reappear a few seconds after either section of the nerve above the testing electrodes, or destruction of the cord. Such a chronaxie, as modified by a central action, may be called the *chronaxie of subordination*.

Chronaxie of subordination is to a great extent governed reflexly, the tension of the muscle concerned being the chief afferent stimulation. According as the foot is either extended or flexed, the chronaxie of the sciatic fibers innervating the gastrocnemius differs; it is shorter when the

foot is flexed and thus the muscle stretched. Stretching the dissected muscle with increasing weights produces in the nerve gradual decrease of chronaxie until a given level is reached. Severing the nerve abolishes any influence of either posture or stretching.

LAPICQUE, L. and M. LAPICQUE (PARIS). Chronaxie of Subordination as Determined by Posture. (Demonstration)

LAQUER, FRITZ (ELBERFELD). Weitere Untersuchungen über das Hypophysenvorderlappenhormon: Prolan.

Der Hypophysenvorderlappen kann bei infantilen weiblichen Nagetieren eine vorzeitige Reifung der Geschlechtsorgane, insbesondere der Ovarien, bewirken. Hierauf haben Zondek und Aschheim ein Testobjekt zum Nachweis des Hypophysenvorderlappenhormons aufgebaut. Sie haben ferner gefunden, dass dieses, von ihnen Prolan genannte Hormon, während der Schwangerschaft im Harn ausgeschieden wird. Hieran anknüpfende Untersuchungen haben ergeben, dass sich junge Ratten in vieler Hinsicht besser zum Nachweis und der quantitativen Auswertung des Prolans eignen als junge Mäuse. Die bisher bekannten chemischen Eigenschaften des Prolans, vor allem seine grosse Empfindlichkeit gegen Säuren und Laugen, sowie seine Unbeständigkeit bei höherer Temperatur, konnten bestätigt werden. Es wurde ferner untersucht, ob das Hormon neben seiner Einwirkung auf die weiblichen Genitalien auch das Wachstum junger Tiere beeinflusst. Hier konnte keine Wirkung festgestellt werden. Auch den Blutzucker von Kaninchen kann das Prolan nicht verändern. Es wird daher angenommen, dass das im Urin der Schwangeren ausgeschiedene als Prolan bezeichnete Hormon nur die auf die Geschlechtsorgane einwirkende endokrine Funktion des Hypophysenvorderlappens, nicht aber seine Wirkungen auf Wachstum und Stoffwechsel umfasst.

LAQUEUR, ERNST (AMSTERDAM). Über Spezifität der weiblichen (Geschlechts-) Hormone im besonderen des Menformons, das Vorkommen im männlichen Individuum und die Standardisierung.

Die Spezifität weiblicher Geschlechtshormone wird teils durch mangelnde Bestimmung des Begriffes "Spezifität," ferner durch zu geringe Betrachtung des quantitativen Momentes bezweifelt. Bei relativ reinen Darstellungen, wie in der Form des Menformons, wobei mit weniger als 0.01 γ bereits gut erkennbare biologische Wirkungen sich hervorrufen lassen, sind die Wirkungen von verschiedenster Bereitungen aus verschiedenster Herkunft ungekünstelt durch Beimengungen von Menformon zu verstehen.—Das Vorkommen im männlichen Organismus von (kleinen Mengen) Menformon, das durch Hervorrufen der wesentlichen "weiblichen" Wirkungen charakterisiert ist, lässt sich erweisen. Für eine genaue Standardisierung auf Grund der ursprünglichen Methode von Allen und Doisy ist die scharfe Definition und Beobachtung der Grenzreaktion erforderlich; hierfür ist die Anzahl und der Zeitpunkt der Beobachtungen (Abstriche) wesentlich; des weiteren ist die Benutzung einer genügenden Menge Tiere und zwar an verschiedenen Tagen (Tagesfaktoren) erforderlich, wobei eine festzusetzende Anzahl die Grenzreaktion erreichen muss, endlich spielt, besonders bei den reineren Präparaten, wie Menformon, die Verteilung der Dosis über eine genügend lange Zeit eine entscheidende Rolle.

LATTES, LEONE (MODENA). **L'eredità delle proprietà individuali del sangue.**

Vi sono attualmente due questioni in discussione circa le proprietà individuali del sangue nell'uomo e alla loro ereditarietà, che ha tanta importanza dottrinale e pratica per la ricerca della paternità.

L'una è quella riguardante i classici gruppi sanguigni, la cui ereditarietà è certa, ma per la quale si discute la modalità della trasmissione. Quattro dottrine sono state proposte: 2 coppie allelomorfe indipendenti (Aa, Bb, Hirszfeld), 2 coppie allelomorfe solidali (linked) con eventuale crossing-over (Kirihaara-Bauer); due coppie allelomorfe completamente solidali (linked) (Furuhata); tre allelomorfi multipli (A, B, R, Bernstein). Le due prime coincidono qualitativamente nelle previsioni, divergono quantitativamente; le due ultime coincidono qualitativamente e quantitativamente.

Per la risoluzione del problema è necessario e sufficiente verificare (con la esclusione del padre) se madri del gruppo O possono avere figli AB, o madri del gruppo AB possono aver figli O. Io coi miei collaboratori abbiamo proseguito questa ricerca; la nostra serie giunge finora (viene ulteriormente proseguita) a 754 coppie madre-figlio tra cui 342 madri O e 34 madri AB. Conformemente ai risultati di Schiff, Thomsen non abbiamo mai trovato figli AB di madre O, nè figli O da madre AB. Ciò è in appoggio alle dottrine di Bernstein e Furuhata e contraddice quelle di Hirszfeld e Bauer, per la quale ultima in realtà sembrano deporre soltanto alcuni casi del tutto isolati, che si prestano a serrata discussione.

Il secondo punto attualmente sottoposto allo studio è quello della ereditarietà di proprietà sanguigne indipendenti dai gruppi e rivelabili solo in via immunitaria. Tali sostanze sono state messe in evidenza col nome di M, N, P, da Landsteiner-Levine e da Schiff, che ne hanno affermato l'ereditarietà. La loro esistenza parrebbe dare un fondamento teorico al recente lavoro di Zangemeister e Krieger secondo il quale nella gravida si manifesterebbero reazioni immunitarie individuali contro le sostanze paterne provenienti dal feto, in modo che con reazioni turbidimetriche nei miscugli dei sieri si potrebbe riconoscere la pertinenza individuale del neonato con la madre (puerpera), col padre e del padre con la madre.

Noi abbiamo cercato di dare una conferma a queste ricerche. Abbiamo escogitato un apparecchio nefelometrico che permette l'esatta correzione cromatica, senza la quale le letture sono inattendibili. Con questo apparecchio abbiamo esaminato numerosi sieri di puerpera addizionati di siero del rispettivo neonato o di neonato estraneo. Abbiamo bensì osservato modificazioni della trasparenza dei sieri, specialmente nel senso dell'aumento progressivo; ma nessun comportamento specificamente individuale tra la madre e il suo proprio figlio.

I risultati di Zangemeister e Krieger, la cui importanza sarebbe stata evidentemente grandissima, non sono stati dunque da noi confermati, e non giungono perciò a dare un sostanziale contributo alla dottrina della eredità della costituzione sanguigna individuale.

LAURENS, HENRY and PAUL C. FOSTER (NEW ORLEANS). **The Ineffectiveness of Carbon Arc Radiation on Anemia in White Rats.**

In rats made anemic by feeding Klim ($12\frac{1}{2}$ per cent by weight in water) from the time they were 21 or 28 days of age, the Hb dropped to about

4 grams per cent in from 2 to 6 weeks. In some rats the Hb fell somewhat lower than this but most of these died. In practically all of the rats the Hb level showed a greater or less tendency to spontaneous recovery. This began after the animals had been on the milk diet for from 4 to 9 weeks, and at the end of 12 weeks the Hb had a value of 8.2 grams per cent as compared with 16 grams per cent in rats of the same age on the stock diet. Our rats show no tendency to breed on the Klim diet and some females, after having been on it for from 9 to 11 weeks, have been placed on the stock diet (Sherman B) and bred with males that had always been on this diet. The Hb of rats from such litters placed on the milk diet dropped to about 4 grams per cent in about 3 weeks instead of in 5 to 6 weeks, but the Hb of these animals also showed a tendency to gradually increase. Such first and second generation anemic rats have been given different amounts of flaming C arc irradiation, small, moderate and massive doses, daily and at certain definite intervals for a total duration of from 2 or 3 weeks to as long as 10 weeks, with no evidence of its having any influence on the rate of Hb regeneration. The size and number of red cells, as well as the ratio of Hb to stroma is not demonstrably altered by the radiation. The rate of growth on the milk diet is almost the same as that of the controls. Excessive irradiation inhibits the growth of anemic rats but, so far as our experience goes, does not influence the growth of rats on the stock diet. Such radiation also has no influence on the rate of regeneration of red cell stroma and Hb in rats made anemic by a series of small hemorrhages.

LEAKE, CHAUNCEY D. (SAN FRANCISCO), A. H. DULMES, D. N. TREWEEK, and ARTHUR S. LOEVENHART (MADISON, WISCONSIN). **The Inhibiting Effect of Sodium Fluoride on Hepatic Lipase.**¹

The inhibiting effect of sodium fluoride on the action of hepatic lipase has been studied *in vitro* by Kastle and Loevenhart,² Loevenhart and Peirce,³ Amberg and Loevenhart,⁴ and Arthus.⁵ We have now obtained evidence that sodium fluoride also inhibits the action of this enzyme *in vivo*.

The average total acidity (determined by titration) in nine experiments on liver breis from normal rabbits was 2.46 cc. N/20 acid resulting from the hydrolysis of the liver fats themselves and from the constant addendum of 0.23 gram of ethyl butyrate. In six rabbits killed by the intravenous injection of 75 to 150 mgm. sodium fluoride per kilogram body weight, there was an average reduction of this normal acidity figure by 67.5 per cent. The *in vitro* addition of constant amounts of sodium fluoride in 1:50,000 concentration to normal liver extracts containing a constant addendum of 0.23 gram of ethyl butyrate resulted in an inhibition of acid formation by 63 per cent as compared with the same liver extracts to which no sodium fluoride was added. The acid conditions of the liver breis containing sodium fluoride added either *in vitro* or *in vivo* returned within an hour

¹ It was originally proposed by Professor Loevenhart to dedicate this little study to the memory of Joseph Hoeing Kastle (1864-1916). It is now appropriate, in view of the untimely death of Doctor Loevenhart (April 19, 1929), to offer it to the memory of these two great scientists, master and pupil.

² J. H. Kastle and A. S. Loevenhart. 1900. Amer. Chem. Journ., xxiv, 491.

³ A. S. Loevenhart and G. Peirce. 1907. Journ. Biol. Chem., ii, 397.

⁴ S. Amberg and A. S. Loevenhart. 1908. Journ. Biol. Chem., iv, 149.

⁵ Arthus. 1902. Journ. de Physiol., iv, 56.

after neutralization, indicating that the sodium fluoride does not destroy this hepatic enzyme.

LEE, M. O. (BOSTON). Some Effects of Long Continued Insulin Administration in Rats.

The effects of continued insulin administration were determined on voluntary activity, blood count, growth, heart rate and oestrous cycle in rats. Insulin was injected twice daily in dosages of 0.1, 0.5 and 1.0 units per 100 grams body weight. Voluntary activity was measured by the revolving cage method with 25 rats. Two periods of one month each with insulin were alternated with two periods of one month without. The voluntary activity was slightly increased during the periods of insulin administration. In 20 rats blood examinations, consisting of erythrocyte, leucocyte and differential leucocyte counts were made. The only deviation in the insulinized rats was a slight increase in eosinophile cells. Growth was slightly accelerated during the first four months of life in a series of 16 insulinized rats as compared with controls. The heart rate in 10 insulinized adult rats averaged 10 per cent lower than the rate in normal animals, when determined 12 or more hours after the last doses of insulin. In normal rats the administration of insulin in doses insufficient to produce convulsions, caused within 2 hours a decrease of 15 to 20 per cent in the heart rate. This decrease was abolished by atropine. These results are interpreted as due to stimulation of the parasympathetic system by insulin, and point towards an antagonistic relation of insulin and adrenalin. The oestrous cycles in insulinized rats were found to be normal, both as to the total duration of the cycles and the duration of the component stages.

LE GOFF, J. M. (PARIS). Cobalt as Vasodilator.

Recently small amounts of cobalt have been found in animal tissues, also in commercial solutions of insulin. The spleen and the pancreas in man are the organs containing the largest quantity of this metal: 2.64 milligrams in the first, 2 milligrams in the second, in one kilo of dry material.¹ I endeavored to gain an idea of the physiological effects of small doses of cobalt on man.

My experiments were conducted first upon rabbits and dogs, afterwards upon 72 human subjects. With the rabbits, 2 to 10 centigrams of cobalt chloride taken daily by mouth with the food during many months do not affect the general health and are partly eliminated in the urine, but the hypodermic injection of 2 to 5 centigrams in an isotonic solution produces a vaso-dilatation of the blood vessels of the ears with a diminution of the blood pressure.

The hypodermic or intramuscular injection of 2 to 5 centigrams of the same compound in human subjects is followed immediately by a redness of the face and the ears, lasting 10 to 15 minutes. Till now, I have made with the same result more than 500 injections (it is remarkable that such a redness does not appear after an injection of the same amount of nickel chloride).

This instantaneous redness of the face seems to be produced by the selective effect of cobalt acting as a possible reagent on the sympathetic system. This striking redness can be obtained also with many organic com-

¹ Science, 1926, 629.

pounds of cobalt such as salicylate, citrate and even cobaltamine. At the same time a fall in the blood pressure can be recorded.

LE GRAND, ANDRÉ (LILLE). De l'action respiratoire de divers sels appliqués directement sur le bulbe rachidien chez quelques mammifères.

LEHMANN, GUNTHER (DORTMUND). Die Abhängigkeit des Energieverbrauchs bei statischer Arbeit von der Muskellänge.

Mit dem Respirationsapparat von *Lehmann-Müller* wurde der Energieverbrauch bei statischer Arbeit der Kniestrecker beider Beine bei Rückenlage der V.P. gemessen, wobei in Höhe der Fussknöchel ein Gewicht von 23 kg befestigt war. Der Energieverbrauch wuchs von der Ausgangsstellung (90° gebeugt) bis zur Streckstellung stetig an. Das Drehmoment von Last + Unterschenkel muss hierbei mit dem Sinus des Deflexionswinkels ansteigen. Es zeigte sich jedoch, dass der Energieverbrauch keineswegs dem Sinus sondern annähernd dem Tangens dieses Winkels proportional anstieg. Nimmt man einen konstanten Energieverbrauch der haltenden Muskulatur pro Einheit der Zeit und Einheit der Haltearbeit an, so wäre dieser Befund nur dadurch zu erklären, dass das Drehmoment der Muskeln umgekehrt proportional dem Cosinus dieses Winkels abnimmt. Die Untersuchungen von *Fick* zeigen, dass das nicht der Fall ist. Die Proportionalität zwischen Energieverbrauch und dem Tangens des Deflexionswinkels kann also nur dadurch erklärt werden, dass der verkürzte Muskel Haltearbeit *unter anderen* Wirkungsgrad ausführt als der gestreckte. Es ergibt sich jedoch keine einfache Proportionalität zwischen Muskellänge und Energieverbrauch für die Einheit der Haltearbeit.

LEHNARTZ, E. (FRANKFURT A.M.). Die fermentative Synthese von Pyrophosphorsäure im Muskelpressaft.

Bereits in früheren Untersuchungen ist gezeigt worden, dass der Phosphatwechsel des Muskels und des Muskelpressaftes in entscheidender Weise von der Natur der anwesenden Ionen abhängig ist, dass es insbesondere gelingt, durch ionale Beeinflussung der den Phosphatwechsel steuernden Fermente anorganische Phosphorsäure zum Verschwinden zu bringen. So wurde zunächst eine Synthese von Hexosediphosphorsäure durch Fluorionen, später eine solche von Phosphokreatin durch Reaktionsverschiebung nach der alkalischen Seite erwiesen. Fernerhin liess sich zeigen, dass auch durch das Adenylsäureion erhebliche Mengen von anorganischer Phosphorsäure zum Verschwinden gebracht werden können. Es zeigte sich vielmehr, dass das unter diesen Bedingungen beobachtete Verschwinden von Orthophosphorsäure auf einer fermentativen Synthese von Pyrophosphorsäure beruht.

Diese Synthese, die im Muskelpressaft verfolgt wurde, tritt bereits bei Adenylsäurekonzentrationen von m/400 auf und erfährt durch Steigerung des Adenylsäurezusatzes noch erhebliche Zunahmen. Das Ausmass der Synthese ist von der herrschenden Reaktion, ihr zeitlicher Verlauf ausser von der Reaktion von der Versuchstemperatur abhängig. Sie erfolgt bereits bei der sauren Reaktion des nativen Pressaftes (pH 5,5-6,00), nimmt mit steigendem pH bis zu einem Optimum von etwa 7,5 zu, um dann an Umfang wieder abzunehmen. Das Maximum der Synthese wird

bei optimaler Reaktion nach sehr kurzer Zeit, bei Temperaturen von etwa 15° z.B. nach, 1 Minute, bei 18–20° gelegentlich nach etwa 15 Sekunden erreicht. Zu nur wenig späteren Zeiten erfolgt wieder ein Nachlassen der Synthese. Die gleichzeitige Verfolgung der anderen bekannten Phosphatfraktionen ergibt, dass gleichzeitig mit der Synthese der Pyrophosphorsäure eine Abnahme der anorganischen sowie der Lactacidogenphosphorsäure und zunächst auch der Phosphokreatinphosphorsäure zu beobachten ist. Mit der Fortdauer der Pyrophosphorsäuresynthese, besonders aber bei der Wiederaufspaltung der synthetisierten Pyrophosphorsäure kommt es jedoch—vor allem bei leicht alkalischer Reaktion—zu einer erheblichen Synthese von Phosphokreatin.—Die Pyrophosphat-synthese kommt nur dem Ion der aus Muskel, nicht dem der aus Hefe gewonnenen Adenylsäure zu.

LEPESCHKIN, W. W. (TUCSON, ARIZONA). **The Structure of Erythrocytes and the Causes of Hemolysis.**

The erythrocytes are generally considered as living cells. Their protoplasm is liquid in its greater part, but its dispersed phases are concentrated in some parts of the cell in such degree that it becomes gelatinous and rigid. These rigid parts of protoplasm form a marginal hoop in the erythrocytes of Birds and Amphibia, but they are not so strongly separated from the liquid protoplasm in the Mammalia. The surface of erythrocytes of every kind is covered by a colorless pellicle which is formed by concentrated phases of the protoplasm and can be liquefied by an absorption of water (dilution of dispersed phases), by an osmotic or mechanical pressure on the cell (mixture of dispersed phases with liquid protoplasm) and by the action of high temperature (decrease of the viscosity). The same factors produce a liquefaction of other rigid parts of the protoplasm. The substances of the liquefied pellicle and other formations mix with the protoplasm in all cases, but the normal pellicle can be restored again. On the whole the protoplasm of erythrocytes represents a colloidal solution with different viscosity in different cell parts. A real stroma is absent; no net or alveolar structure is observed, nor "Plasmamembran." The so called stroma which remains after the plasmolysis produced by poisons is the pellicle. The absorption of water brings about the disappearance of the pellicle, but protoplasm diluted with water produces an adsorption film (haptogene membrane) which remains after the hemolysis. The pellicle is of no importance for the hemolysis. It is easily permeable to hemoglobin which does not come out from the cell even if the pellicle disappears completely. The cause of hemolysis is not the bursting or softening of the pellicle but a chemical change in the protoplasm of the erythrocytes. All substances which produce any chemical change in the principal chemical compounds composing this protoplasm, that is, hemoglobin or lipoids, bring about hemolysis. It is very probable that hemoglobin and lipoids are combined with each other in the protoplasm of erythrocytes, but their chemical compound is very unstable. It can evidently be decomposed even by a slight chemical change, by high temperature, strong light and purely mechanical effects. The temperature coefficient of hemolysis produced by high temperature and narcotics which bring about the denaturation of hemoglobin is exactly the same as the coefficient of the denaturation itself. This proves that the chemical change of hemoglobin but not that of the colorless pellicle brings about the hemolysis.

LIDDELL, H. S., O. D. ANDERSON, and W. T. JAMES (ITHACA, NEW YORK).

An Examination of Pavlov's Theory of Internal Inhibition.

On the basis of the defensive reaction to an electric shock conditioned reflexes were established in the sheep. This animal, because of its docility and the simplicity of its behavior as compared to the dog, is a favorable subject for the study of these reflexes. In recording the development of the various types of conditioned response described by Pavlov, observations were made which appear to support his theory of internal or cerebral inhibition.

According to this theory the inhibitions involved in discrimination of stimuli, and in delayed and trace conditioned reflexes, are identical. Moreover, a given brain can develop only a certain quantity of this inhibition. When a new adjustment requiring inhibition becomes necessary a mobilization of inhibition occurs to supply the need. As a result, an insufficient quantity is available for previously established negative responses and these are temporarily weakened. In a sheep which discriminated perfectly between an electric bell and a buzzer the formation of a delayed response to the metronome disturbed this differentiation and both bell and buzzer evoked a positive reaction. When the delayed reflex developed further, the bell-buzzer differentiation was fully restored.

If the new adjustment requires inhibition beyond the brain's capacity to supply it, the equilibrium between excitation and inhibition may suffer a more or less prolonged disturbance in the direction either of hyperexcitability or of somnolence. Pavlov refers to these abnormal states as experimental neuroses. We have observed three clearly defined instances of similar disturbances in sheep. These animals were thoroughly trained and performed with precision before the "neuroses" developed. In one case, when the delayed reflex to the metronome had been gradually extended to thirty seconds the delay, after a period of fluctuation, entirely disappeared and the animal developed an acute state of hyperexcitability which has persisted for seven months. According to Pavlov's theory, the longer the delay, the more inhibition is required. This state might be attributed, therefore, to the demand for more inhibition than could be supplied.

A pathological deviation of the equilibrium point between excitation and inhibition may also occur in the dog if cerebral excitation follows inhibition too quickly. A "neurosis" was observed in a sheep when delayed reflexes of five seconds' duration followed at intervals of thirty seconds to one and one-half minutes. That the summation of excitations evoked by the electric shock is not the cause of these "neuroses" in the sheep is established by the fact that repeated shocks do not produce any such disturbance and that our third instance of prolonged hyperexcitability followed closely upon the presentation of a long series of inhibitory conditioned stimuli.

Our results do not support Pavlov's conception of sleep as summation and irradiation of internal inhibition. Many extinctions of conditioned reflexes through repetition of the conditioned stimulus without the electric shock have failed to elicit any signs of somnolence.

The respiration has proved to be a delicate and reliable indicator, not only of the investigatory reflex aroused by a new stimulus, but also of the developing conditioned reflex.

LIDDELL, H. S., O. D. ANDERSON and W. T. JAMES (ITHACA, NEW YORK).
Cinema Demonstration of Conditioned Reflexes in the Sheep.

LIEBEN, F. in collaboration with E. MOLNAR (VIENNA). **On the Break-down of Some Physiologically Interesting Substances by Oxidation after the Method of Hehner.**

The effect of oxidation after the method of Hehner (used for glycerol determination) on different substances was studied.—The oxidation of N-free carbohydrates and glucosamine amounts to 100 per cent, other carbohydrates (containing N) were incompletely oxidized.—The oxidation of some well known cyclic substances was investigated.—We inquired then about the behaviour of amino acids and compared in the first place the progress of oxidation (Hehner value) with the progress of deamination (Kjeldahl value).—From this point of view the amino acids could be divided into 3 groups. In the first group the two values were found to be nearly equal, in the second the "Kjeldahl value" is markedly higher than the "Hehner value," in the third the contrary is the case. This behaviour must be dependent on the intermediary products of oxidation; we had therefore to inquire into the behaviour of all possible intermediary products (mono- and dibasic acids, hydroxyacids) toward the oxidation after Hehner. This inquiry justified the fore-mentioned classification of the amino acids. Some of these intermediary products could be detected by steam-distillation following the oxidation process.—Some proteins were also investigated and found to show all about the same behaviour. They were deaminized on a scale of 50 to 70 per cent, the "Hehner value" is rather lower; the oxidation of casein reaches its maximum after five hours and does not surpass 75 per cent of the value for total oxidation.

LILLIE, R. S. (CHICAGO). **Circuit Transmission and Interference in Passive Iron Wires. (Demonstration)**

LIM, R. K. S., S. M. LING, W. C. MA, T. G. NI and T. C. SHEN (PEPING).
The Metabolism of the Stomach.

1. *The mitochondria-Golgi complex during secretory elaboration and discharge.* During the elaboration of secretion, the mitochondrial substance dissociates into a secretion component and free lipid (Golgi material). Part of the Golgi lipid is extruded with the fluid secretion derived from the secretion component. In the peptic cell the secretion component normally passes through a semi-solid storage phase (zymogen granules), before being discharged as a fluid, but after prolonged stimulation (12-24 hours), the peptic secretion may be discharged without storage (*i.e.*, granule formation). In the oxyntic cells, there is no storage phase.

2. *Lipoid content of gastric juice and mucosa during secretion.*

Juice. This contains lipid of which not more than 10 per cent is phospholipin; the lipid output increases with secretion.

Mucosa. The mucosa contains about 3 per cent of lipid of which less than half is phospholipin. After 6 hours' continued secretion, the total lipid remains unchanged but the phospholipin fraction and the iodine numbers of both the P (202 to 369) and non-P (182 to 251) fatty acids increase.

3. *Gas metabolism during secretion (observations on vivi-perfused stomach).* During secretion the consumption of oxygen and sugar is

generally but not invariably increased. In the phlorizinised or diabetic stomach, O_2 consumption follows a normal course during secretion, but sugar intake is not increased and may be depressed. Neither of these conditions affects the ability of the stomach to secrete or to contract.

Under resting conditions, the oxygen intake does not usually suffice to oxidise all the sugar, but during secretion oxygen is absorbed in excess over sugar.

The R.Q. of the *vivi*-perfusion experiments is variable; the mean value is below 1.0. In preliminary experiments on the mechanically perfused (Dale-Schuster pump) resting stomach, the R.Q. was found to be about 0.79. The evidence here presented is taken to indicate that the mitochondria-Golgi complex is probably the source of the lipid which is apparently oxidised during glandular metabolism.

LINTZEL, W. (BERLIN). *Über die Resorption des Eisens.*

Legt man zu einer Nahrung mit konstantem Eisengehalt eine grössere Menge Eisen in Form von Ferrichlorid oder Ferrosulfat zu, so wird eine bestimmte Eisenmenge retiniert. Die retinierte Menge war in Versuchen am Menschen unabhängig von der Oxydationsstufe des Eisens. Vermutlich wird Ferriion im Magen reduziert, sodass die Resorption in Form von Ferroion erfolgt. Die Eisenretention bleibt aus, wenn Komplexverbindungen wie Ferrocyankalium oder Blutfarbstoff dargeboten werden. Eine besondere Betrachtung erfordern Komplexverbindungen des Eisens wie Citrat, Tartrat etc., die durch die Magensalzsäure leicht gespalten werden. Diese werden retiniert wie einfache Salze. Gibt man jedoch gleichzeitig einen Ueberschuss der komplexbildenden Säure, so können die Komplexverbindungen des Eisens im Dünndarm regeneriert werden, und es wird kein Eisen retiniert. Die einfache Formel für die Resorption löslicher Eisenverbindungen lautet: Ionisiertes Eisen wird resorbiert, komplexe Eisenverbindungen dagegen nicht. Dies Resultat hat sich in Ansatzversuchen an jungen Tieren bestätigen lassen. Die Verfütterung komplexbildender Säuren erzeugt Anämie.

Die Magensalzsäure verhindert die bakterielle Bildung von Säuren im Magen, die die Eisenresorption im Dünndarm hemmen würden. In den unteren Darmabschnitten treten dagegen derartige Stoffe auf. So erklärt sich die alte Tatsache, dass die Eisenresorption auf die oberen Darmabschnitte beschränkt bleibt. Die Versuche werfen ferner Licht auf die Ursachen der Milch-anämie der Säuglinge. Die in jeder Milch vorhandene Citronensäure, vielleicht auch andere Säuren des Milchfettes, hemmen die Resorption der geringen Eisenmengen, die bei überwiegender Milchkost zugeführt werden.

LIPOW, E., WILLIS K. WEAVER and C. I. REED (CHICAGO). *Effects of Ether Anesthesia on the Inorganic Constituents of the Blood.*

As a preliminary to a study of the influence of the autonomic system on the inorganic blood constituents, it was necessary to establish the magnitude and direction of alterations induced by ether anesthesia in dogs. Observations extended over two hour periods. In fourteen experiments, it was found that plasma calcium was increased markedly in two animals with initial concentrations below 9 mgm. per 100 cc. In two there was a decrease during the first half hour, with an increase above the initial level during the second hour. In the other ten, there was a progressive fall.

In fourteen determinations of inorganic phosphorus, the end result was invariably a pronounced increase, with minor fluctuations during the first hour in five cases. Magnesium varied greatly in the course of experiments and there was no constancy among different animals. Potassium showed a tendency to decrease during the first hour, followed by a pronounced increase during the second hour, frequently above the initial level. Sodium generally decreased slightly during the first hour, followed by a progressive increase. In two instances the increase was apparent at the end of the first half-hour.

LOEBEL, R. O., E. SHORR and H. B. RICHARDSON (NEW YORK). **The Respiratory Metabolism of the Tubercle Bacillus.**

In the study of tuberculosis it is desirable to know the processes by which the parasite obtains energy and the influence of adverse conditions on its respiratory metabolism.

The following is a study of the oxygen consumption of the tubercle bacillus as influenced 1, by the age of the culture; 2, by the constituents of the nutrient medium, and 3, by the pH of the solution.

After 8 days' cultivation on Long's synthetic medium the consumption of oxygen, measured in the micro-respiration apparatus of Warburg, averaged 2.6 cu.mm. per mgm. of moist weight, per hour; after 15 days, 2.2; after 22 days, 0.45; and after 29 days practically zero. The maximum was about twice as much as reported for mammalian leucocytes. It was about $\frac{1}{2}$ that of a rapidly growing organism of the acid-fast group; *i.e.*, the smegma bacillus.

In order to establish a base-line for the study of nutrients, the organisms were transferred from Long's medium to a similar solution containing only the salts of sodium and potassium. After 6 days the breathing became much reduced, but on retransfer to Long's medium regained nearly its original level. The oxygen consumption in Long's medium could be fractionated as follows:

	per cent
Starvation level	5.8
Effect of glycerol	73.0
Effect of nitrogenous substances (asparagin and amm. citrate)	19.2
Effect of ferric amm. citrate and magnesium sulfate	2.0

After starvation the organisms retained their original power of growth.

No increase in breathing above the starvation level was observed as the result of transfer from buffered saline to a similar solution containing 5 per cent glucose or levulose. This is in accord with the well known difficulty of cultivating the organisms by the use of sugars. Sodium lactate caused a rise which even exceeded the effect of glycerol, but was entirely ineffective as a substitute for glycerol in the promotion of growth. This is an instance in which the energy metabolism is dissociated from growth.

In phosphate mixtures the oxygen consumption for short periods was much the same over a range extending from pH 1.5 to pH 12.0.

In the presence of glucose the anaerobic glycolysis was increased by 0.022 mg. of lactic acid per 100 mg. of bacteria per hour. This would supply less than 1 per cent of the energy which was obtained by oxidation of Long's solution.

TABLE 1
Influence of foodstuffs on growth and respiration of the tubercle bacillus—H 37

OXYGEN CONS.	NO FOOD- STUFFS	GLYCEROL 5 PER CENT	Na LACTATE 5 PER CENT	GLUCOSE 5 PER CENT	LEVU- LOSE 5 PER CENT	REMARKS
<i>hours</i>						
1	1.1	1.8	2.1	1.3	1.2	16 d. cult. 2 d. starv.
1	0.6	1.5	2.4	0.9	0.5	16 d. cult. 6 d. starv.
1	1.0	1.2	1.6	0.9	0.7	15 d. cult. 2 d. starv.
2	1.8	2.4	3.3	1.8	1.5	15 d. cult. 2 d. starv.
Growth	None	Profuse	None	Fair	None	Each foodstuff added to Long's medium minus glycerol

TABLE 2
Influence of hydrogen ion concentration on respiration of the tubercle bacillus—H 37

O ₂ CONS.	pH 1.5	pH 5.6	pH 7.4	pH 8.8	pH 12.0	PHOSPHATE BUFFERS M/150
<i>hours</i>						
1	1.0	1.0?	1.1	1.1	1.2	16 d. cult. 2 d. starv.
1	1.3	1.6	1.6	1.4	1.5	10 d. cult.
2	2.3	3.3	2.8	2.6	2.8	10 d. cult.
3	3.3	5.1	4.4	4.0	4.3	10 d. cult.
1		1.7	1.8	1.5		10 d. cult.

LOHMANN, K. (BERLIN-DAHLEM). Über die Pyrophosphatfraktion im Muskel.

Die im Muskel vorhandene, autolytisch und in heisser Säure leicht zu o-Phosphat aufspaltbare P-Verbindung (Pyrophosphatfraktion) liegt in chemischer Bindung an Adenylsäure vor. Die Abspaltung des Pyrophosphats aus dieser Verbindung erfolgt spontan schon bei Zimmertemperatur aus dem in Wasser schwer löslichen Ba-Salz bei neutraler Reaktion. Die biologische Bedeutung dieser Adenylpyrophosphorsäure für die Kohlenhydratspaltung des Muskels und der Hefe wird besprochen.

LÖHNER, L. (GRAZ). Über Nachweis und Wirkungsweise der Gallen-amylase.

Nach moderner Auffassung wird die Abscheidung der Galle durch die Leber, die sogenannte Cholerese, als ein der Diurese vergleichbarer Exkretionsvorgang aufgefasst; hinzugefügt wird allerdings, dass dieses Exkret verdauungsphysiologische Aufgaben durch eine besonders die Fettver-

dauung beeinflussende Milieuwirkung erfülle. Im Zusammenhange mit diesem Standpunkte wird neuestens das Vorkommen von Enzymen in der Galle völlig geleugnet.

Verf. konnte in Bestätigung alter Angaben (v. Wittich¹) u.a. den Nachweis erbringen, dass die Galle aller von ihm untersuchten Säugetierarten (Hund, Katze, Rind, Schaf, Schwein, Kaninchen, Meerschweinchen) unzweifelhaft eine Amylase enthält, wenn auch der Gehalt nach Art und Individuum ausserordentlich schwankt. Während nach Gallenzusatz nichtverkleisterte Stärkesuspensionen kaum angegriffen werden, zeigen Kleisterlösungen, besonders aber Dextrinpräparate und der amylopektinreiche Bodensatz der nach dem Biedermann'schen² Verfahren hergestellten Amyloselösungen deutlichen Abbau und Verzuckerung. Schon daraus geht hervor, dass die Galle auch als echtes Verdauungsekret anzusehen ist. Sie nimmt an der Dünndarm-Kohlenhydratverdauung, besonders in den vorgeschrittenen Phasen, direkten Anteil; dazu kommt noch die bekannte indirekte Wirkung durch Aktivierung (Amylokinase) und Förderung der Pankreasamylase in ihrem Leistungsvermögen.

LOMBARD, WARREN P. (ANN ARBOR). **The Surface Tickle Sense of the Human Skin.**

I wish to retract or at least modify the statement which I made at the meeting of the American Physiological Society, 1912, and at the IXth International Congress of Physiologists, 1913, that "certain spots on the skin respond to mechanical, point excitations by tickle, and other points by touch sensations." Evidence which I am now obtaining in an examination of the area previously studied makes it probable that although certain spots quite uniformly give tickle, and other spots pressure, there are many spots which give tickle, touch, or pressure sensations according to the condition of the peripheral and central nervous mechanisms at the time.

LOONEY, JOSEPH M. (PHILADELPHIA). **The Preparation of Colloidal Carbon. (Demonstration)**

LUCAS, G. H. W. and V. E. HENDERSON (TORONTO). **The Effects of Cyclopropane as an Anaesthetic.**

A new anaesthetic gas, cyclopropane, was prepared in the course of a study of the possible sources of toxicity in propylene. The authors have subsequently learned that according to Papin and Ambard, cyclohexane has anaesthetic properties. Cyclopropane produces anaesthesia of surgical degree in cats in a concentration of 11 per cent in oxygen. For induction about 15 per cent may be used for a minute or two. Anaesthetization is rapid, with little or no struggling and recovery takes place almost equally rapidly. With anaesthetic concentrations the blood pressure rises slightly or remains normal, respiration is of a normal rate and depth. Twenty-five per cent and 30 per cent causes a decrease in blood pressure and in respiration both of which are quickly recovered from if the anaesthetic is removed.

The animals have been anaesthetized on three successive days for periods of two hours without showing any apparent subsequent toxic effects.

¹ v. Wittich, *Pflüger's Arch. f. Physiol.* 3, 1870, 339-352.

² W. Biedermann, *Fermentforschung*, 1, 1915, 389.

The oil water coefficient is approximately 61. One hundred cubic centimeters of olive oil at 37°C. dissolve 1030 cc. gas and 100 cc. water dissolve 16.8 cc. The gas as prepared is contaminated with 8 per cent of a mixture of hydrogen and a hydrocarbon. This contaminating gas showed no anaesthetic action when 30 per cent was given in oxygen. The high anaesthetic power of this gas has enabled us to make a study of the action of an anaesthetic on acid-base metabolism under the most favorable conditions.

LUCK, JAMES MURRAY, VEON CARTER KIECH, and LEWIS SPECKER (STANFORD UNIVERSITY, CALIFORNIA). **The Catabolism of Amino Acids.**

The most acceptable theories of protein catabolism postulate the oxidative or hydrolytic deamination of amino acids. The nitrogen is believed to be converted into urea which is commonly regarded as the principal nitrogenous end product in mammals. Little, if anything, is definitely known about the intermediate steps. If these are negligible in nature, or if the possible intermediate compounds have only an ephemeral existence the decrease in amino nitrogen following the injection of amino acids into animals should keep pace, quantitatively, with the increase in urea nitrogen.

We have approached the problem by applying to groups of animals which have received amino acids by subcutaneous injection the methods of tissue analysis. Standard white rats in groups of 9 or 10 were used. Six or 7 of these were simultaneously injected with the experimental substance, the bladders were promptly emptied, and the subjects were placed in small individual metabolism cages. The remaining 3 or 4, injected with physiological saline, served as controls. At appropriate intervals up to 12 hours after injection, the animals were killed and each carcass including any urine voided within the time was analyzed for amino acid nitrogen and urea.

After the administration of d. glutamic acid and dl. alanine (0.3-0.4 gm. nitrogen per kilo), the amino nitrogen content of the animal fell to the normal level within 4 to 6 hours. Glycine decreased much more slowly. Following the injection of l. histidine and d. arginine the amino nitrogen decreased very slowly, remaining unchanged in the latter instance for over 7 hours.

In the case of every amino acid investigated (except arginine), the increase in urea set in so slowly that for the first 4 or 5 hours urea formation lagged behind the amino nitrogen disappearance by as much as 50 per cent. Even after complete disappearance of the amino nitrogen of injected alanine only 60-70 per cent of the expected amount of urea had been formed. It therefore follows that the first phase of the catabolism of injected amino acids is characterized by a depression in the rate of endogenous protein metabolism or by the formation of nitrogenous intermediates in which the nitrogen is present neither as urea nor as primary amino nitrogen.

In other groups of animals, similarly injected, blood, muscle, and liver were separately analyzed. Apart from quantitative differences in the effects produced by different amino acids, we were interested to observe that during the initial period of rapid amino acid disappearance and delayed urea formation, the injected amino acids are resident primarily in the liver. Migration into the skeletal muscle proceeds more slowly.

LUCKHARDT, ARNO B. and MARY MONTGOMERY (CHICAGO). **The Mechanism of Reinforcement of the Knee Jerk in the Human Subject by a New Procedure.**

Many maneuvers exist for the reinforcement of a sluggish knee jerk. The difficulties of some maneuvers consist in proper timing of the reinforcing act lest inhibition result (Jendrassik); in others, the observer is never certain that the subject executes the act while the blow is applied to the patellar ligament (clenching fists).

Method. Any sustained effort of the human subject (except contraction of the muscle groups antagonistic to the quadriceps extensor) if continued through the period during which the patellar ligament is being struck, reinforces the knee jerk as determined by the increased height of the mechanogram obtained by the Johnson knee jerk apparatus.¹ The simplest and most practical maneuver involving sustained effort consists in a horizontal extension of the arm alone (at right angles to the body) or supporting some weight, e.g., a moderately heavy book. The knee jerk is exaggerated promptly, and the accentuation thereafter increases regularly and progressively with fatigue.

Mechanism. It is believed that the reinforcement under these conditions is due to an increase in tone of the quadriceps as a result of an overflow of motor impulses to the knee jerk center; for 1, accompanying the increase in the height of the knee jerk there occurs an involuntary extension of the leg, and 2, slight voluntary extension of the leg from which the knee jerk is taken results in a great exaggeration of the response (as Hoffmann² found by galvanometric registration in studying other tendon reflexes).

LULLIES, H. (KÖNIGSBERG). **Experimentelles zur Theorie der elektrischen Reizung.**

Der Theorie von *Nernst* liegt die Annahme zu Grunde, dass ein elektrischer Strom dann erregend wirkt, wenn er in den polarisierbaren Grenzflächen des Gewebes eine Konzentrationsänderung von bestimmtem Betrage hervorruft. Die direkte Messung von Polarisation und Schwellenstromstärke zwingt dazu, diese Annahme zu Gunsten einer anderen Beziehung aufzugeben, zumal die *Nernst'sche* Theorie gerade den wichtigsten Tatsachen der Reizphysiologie nur mit Hilfe mehr oder weniger begründeter Hypothesen gerecht werden konnte.

Es lässt sich mit geeigneten Methoden feststellen, wieviel von einem veränderlichen Strom, der ein Gewebe durchfließt, an polarisierbaren Grenzflächen für eine Konzentrationsänderung in Frage kommt, und wieviel in unpolarisierbaren Nebenschlüssen vorbeiströmt. Messungen an Froschnerven mit sinusförmigen Wechselströmen sehr verschiedener Frequenzen (20-300,000 p. Sek.) ergaben, dass die Reizschwelle dann überschritten wird, wenn die innere Polarisationskapazität des Nerven mit einer gewissen Elektrizitätsmenge *Q* aufgeladen ist; das bedeutet eine bestimmte notwendige Gesamtkonzentrationsänderung an der Grenzfläche. Diese Beziehung gilt von den höchsten anwendbaren Frequenzen bis zu etwa 200 Wechsell. p. Sek. Unterhalb dieser Grenze wird die notwendige Elektrizitätsmenge grösser. Dieses Verhalten bei niedrigen Frequenzen

¹ C. A. Johnson. Amer. Journ. Physiol., 1927, lxxii, 75.

² Paul Hoffmann. Untersuchungen über die Eigenreflexe. Berlin, 1922.

wird verständlich und quantitativ erklärt durch die naheliegende Annahme, dass die Konzentrationsänderung, die sich bekanntlich bei niedrigen Frequenzen immer tiefer in den Elektrolyten hinein erstreckt, physiologisch wirken kann nur soweit und solange sie in eine bestimmte Schicht d an der Grenzfläche fällt. Bei hinreichend langsam ansteigenden Strömen kann die Konzentration in dieser Schicht dauernd unterhalb der Schwellenkonzentration bleiben ("Einschleichen"). Q beträgt für den Froschischidiacus $1-2 \cdot 10^{-10}$ Coulomb, die Schichtdicke d errechnet sich zu $1-3 \cdot 10^{-4}$ cm.

Dieses zunächst nur für Wechselströme abgeleitete Erregungsgesetz lässt sich mittels einer besonderen Messanordnung auch für die andern gebräuchlichen veränderlichen Reizströme, z. B. rechteckige Stromstöße und Kondensatorentladungen prüfen und bestätigen: Es wird die jeweilige Stromstärke im Nerven während des Fließens des Reizstromes bestimmt, indem durch ein Helmholtz'sches Pendel zu verschiedenen Zeiten nach Beginn des Reizstromes dieser für eine möglichst kurze Zeit (10^{-6} Sek.) in ein hochempfindliches Elektrometer geleitet wird. Die so gemessene Stromstärke beträgt in der ersten 100.000stel Sekunde das 1,5-2fache der Endstromstärke. Durch graphische Verfahren erhält man die bei verschiedenen Reizspannungen für das Wirksamwerden eines Reizes eben notwendige "gespeicherte" Elektrizitätsmenge. Diese ist in der Tat weitgehend konstant. Sie nimmt gesetzmässig zu, sobald bei niedrigen Reizspannungen und entsprechend langen Reizzeiten rechnungsgemäss ein merklicher Teil der Konzentrationsänderung nicht mehr in die massgebende Schicht d fällt.

Die mathematische Darstellung der Theorie mit Hilfe der verschiedenen direkt messbaren Konstanten ist relativ einfach. Ihrer Ausdehnung auf andere Gewebe scheinen keine Bedenken im Wege zu stehn. Jedenfalls ist sie weitgehender experimenteller Prüfung zugänglich.

LUSK, GRAHAM and WILLIAM H. CHAMBERS (NEW YORK). Specific Dynamic Action in the Normal and Phlorhizinized Dog.

A normal dog, the basal metabolism of which was 21.8 calories per hour, showed an increased metabolism of 3.5 per cent during the 3rd to the 5th hours after giving lard, 10 grams. The metabolism increased by 15 per cent when lard, 10 grams, plus glutamic acid, 20 grams, were administered. The increase was 48 per cent when the dog received 300 grams of meat. The same dog, rendered diabetic with phlorhizin, showed a maximal increase in basal metabolism of 35 per cent. The metabolism did not increase when fat, 10 grams, was administered, nor did it increase after the dog received lard, 10 grams, plus glutamic acid, 20 grams. Although the glucose output was increased in the urine, due to the formation of glucose from glutamic acid, this was not accompanied by an increased heat production, as is the case when the glucose formers, glycine and alanine, are ingested by the normal or phlorhizinized dog. When meat, 300 grams, was given to this diabetic dog the respiratory quotient remained at the diabetic level of 0.700, while the total metabolism rose only 15 per cent above the basal metabolism as measured during the preceding hours. However, the metabolism reached the same height which it had achieved after giving meat to the dog when it was normal. This may be due to the fact that the protein metabolism in the two instances was not very different.

LUTZ, BRENTON R. (BOSTON). **Reflex Cardiac and Respiratory Inhibition in the Elasmobranch Fish, *Scyllium canicula*.**

In Elasmobranchs reflex cardiac inhibition has been described as subordinate to reflex respiratory inhibition arising from sensory stimulation of some part of the respiratory apparatus. The present report presents evidence which indicates that a great variety of afferent pathways may be involved, and that while generally the cardiac and respiratory centers are inhibited together the former is not subordinate to the latter, and each may be inhibited independently.

In all cases the forebrain was destroyed and the cord was transected at various levels and pithed posteriorly. The heart rate and respiration were recorded by means of hooks, threads, and levers. The gills were perfused through the mouth.

Cardiac and respiratory arrest were obtained on sensory stimulation of the skin, nasal organ, gills, pericardial walls, surface of the ventricle, and parietal peritoneum, and also by electrical stimulation of the central end of the vagus, hypobranchial, and lateral line nerves.

Sensory stimulation of the mesentery, wall of the stomach, and spiral valve caused cardiac and respiratory inhibition even when the cord was destroyed posterior to the second vertebra, but not when the vagi were cut posterior to the origin of the cardiac branches. The afferent pathway from these viscera is in the vagus and not in the sympathetic system and cord since neither cardiac nor respiratory arrest can be obtained on stimulation of the first sympathetic ganglion when the spinal cord is intact, but can be elicited on stimulation of the stomach, spiral valve, and mesentery when both cord and sympathetic ganglia are destroyed.

Cardiac and respiratory inhibition were obtained for over twenty-four hours when the gills were perfused; for over three and one-half hours without perfusion but with intact circulation; and for over one hour when there was neither perfusion of the gills nor blood supply to the medulla.

MACALLUM, A. B. and W. R. CAMPBELL (LONDON, ONTARIO). **The Secretion of "Acid" by the Kidney.**

When 5 to 8 cc. of a solution of 1 per cent ferric ammonium citrate and 0.8 per cent sodium ferrocyanide are injected intravenously per kilo in the dog, cat, or rabbit, Prussian blue is excreted in the urine if the animal has been without food for some time but if fed an hour or so before the injection is made, the salts injected appear unchanged in the urine ("alkaline tide"). Examination of the kidneys of such animals excreting Prussian blue indicates that it is formed only in the cells of the proximal convoluted renal tubules which pass it out into their lumina. The formation of the blue is not due to the action of sodium dihydrogen phosphate, the salt chiefly responsible for the acid reaction of the urine, for when a portion of the solution used for injection is added to acid urine no Prussian blue is formed nor is it formed when a quantity of the solution is added to a saturated solution (pH 3.8) of sodium dihydrogen phosphate except slowly after some hours.

The facts ascertained make it evident that in the cells of the proximal convoluted renal tubules the acid which brings about the formation of Prussian blue is hydrochloric, formed as it is in the parietal cells of the peptic tubules when they are secreting acid (Collip):



The acid is passed into the lumina to react there with any disodic hydrogen phosphate of the glomerular filtrate, converting it into the sodium dihydrogen phosphate of the urine, while the disodic salt formed in the cells of the tubules probably diffuses into the lymph and blood to maintain the normal acid-base balance therein.

In the cells of the proximal convoluted renal tubules the reaction involved in the formation of the acid is the same as that involved in the formation of hydrochloric acid by the parietal cells of the gastric tubules. When the latter are in action the disodic hydrogen phosphate is formed in excess, consequently the acid formation in the cells of the proximal renal tubules ceases and the urine is then alkaline.

MACHEBOEUF, M. (PARIS). Sur l'état physico-chimique de la lécithine et des esters de cholestérol dans le sérum et le plasma sanguins.

Le sérum et le plasma sanguins sont limpides, ils contiennent cependant de la lécithine, du cholestérol et des esters de cholestérol; ces substances peuvent donner avec l'eau, des émulsions, mais jamais de solution limpide. On a remarqué de plus qu'il est impossible d'extraire du sérum la totalité des lipides par simple agitation avec de l'éther.

Les globulines n'entraînent, lors de leur précipitation par le sulfate d'ammonium, qu'une faible fraction de la lécithine et du cholestérol.

L'auteur a soumis les albumines à une série de précipitations fractionnées par variation de la concentration des ions H^+ en présence de quantités variables de sulfate d'ammonium. Dans la fraction la plus facilement précipitable par acidification se sont rassemblés la lécithine et les stérides; après plusieurs précipitations cette fraction s'est montrée réfractaire à un fractionnement ultérieur; la substance ainsi obtenue est constituée par 23% environ de lécithine, 18% d'esters de cholestérol, 59% de protéides et des traces de cholestérol libre. Malgré cette très haute teneur en lipides cette substance est très soluble dans l'eau en milieu neutre ou alcalin; il est ainsi possible d'obtenir des solutions limpides contenant, par litre, plus de 50 g. de lipides, voire des gélées limpides en contenant plus de 100 g. Ces solutions ne livrent pas leurs lipides à l'éther et l'alcool froid en coagule mal les protéides; pour séparer complètement les lipides des protéides il faut traiter les solutions par de l'alcool bouillant, puis épuiser le coagulum à l'éther. Les lipides ainsi séparés n'ont plus la propriété de se dissoudre dans l'eau (même en milieu alcalin), ils peuvent seulement donner avec l'eau des suspensions laiteuses et instables dont l'éther enlève facilement les lipides.

MACHEBOEUF, M. A. (PARIS). Sur l'état physicochimique de la lécithine et des esters de cholestérol dans le sérum et le plasma sanguins. (Démonstration)

MACHT, DAVID I. (BALTIMORE). Contributions to Phytopharmacology or the Applications of Plant Physiology to Medical Problems.

The author, for a number of years, has been carrying on general pharmacological studies on the comparative reactions of animal and plant protoplasm to various drugs and poisons, which made it evident that living plant tissues may react very differently to certain drugs from animal tissues to the same substances. Frequently, a drug of plant origin is more poison-

ous for animals than plants and, vice versa, toxins of animal origin are very much more poisonous for living plant protoplasm than for living animal protoplasm. Such work has been carried on especially on the growth of roots of various seedlings but also on the growth of stems, transpiration of water through stomata of leaves, etc.

By such phytopharmacological methods, there was demonstrated the presence of a toxin in the blood, saliva, milk, sweat, and other secretions of menstruating women. Further studies gave the first experimental demonstration of the presence of a toxin in the blood of pernicious anemia, which is not present in secondary anemia, carcinoma, leukemia, and other blood conditions. This discovery furnishes a valuable method for differential diagnosis of pernicious anemia and a quantitative method for evaluation of various therapeutic procedures.

The author announces in the present communication the discovery of a toxin in the blood of pemphigus, noted by Dr. I. Pels and himself while studying numerous specimens of blood from dermatoses. Announcement is also herewith made of the presence of a toxin in the blood of leprosy, which serves to differentiate leprosy from blood sera of tuberculosis and syphilis and led to an important discovery in regard to its therapy.

Further observations to be reported are on the blood of malaria, eclampsia sera, and on the extreme toxicity of certain animal poisons—of the toad, bee, ant, and particularly, snake venoms.

MACNIDER, WILLIAM DEB. (CHAPEL HILL, NORTH CAROLINA). **The Nephrotoxic Action of Repeated Injections of Uranium Nitrate in the Dog. A Functional and Pathological Study.**

1. Initial subcutaneous injections of 2 to 4 mgm. of uranium nitrate per kilogram induce in the dog an acute nephritis in which the major injury is epithelial in character. The glomeruli as shown anatomically by reparative changes participate in the acute injury.

2. The functional expression of this type of injury is shown by the animals becoming polyuric with an albuminous urine containing numerous granular casts. The elimination of phenolsulphonethalein is rapidly reduced and the reserve alkali of the blood is depleted. There then develops a retention of urea nitrogen, non-protein nitrogen and creatinine.

3. The repair of the acute uranium injury is characterized by a regeneration in the convoluted tubules of two types of epithelial cells: a specialized type normal for this portion of the tubule, and a flattened, non-specialized type. The glomeruli show connective tissue obliterative changes which vary in character and severity with the duration of the stage of glomerular repair.

4. These anatomical changes are associated with a decrease in the volume output of urine, amount of albumin and number of casts. There is an increase in the elimination of phenolsulphonethalein, an increase in the reserve alkali of the blood, and a decrease in the retention of urea nitrogen, non-protein nitrogen, and creatinine.

5. The functional and anatomical response of such animals to a second intoxication by uranium nitrate has in part depended upon the type of epithelial repair. If the dominant type of repair to the convoluted tubules consisted in a replacement of the specialized epithelium of the convoluted tubule type the animals failed to show functionally any protection to a

second uranium nitrate injection. The epithelium became necrotic. If the tubular repair had in large measure been effected by a relining of the tubules by a flattened, non-specialized type of cell the second injection of uranium gave less evidence of a renal functional disturbance. The elimination of phenolsulphonephthalein and the reduction in the reserve alkali of the blood were less marked, and the retention of urea nitrogen, non-protein nitrogen and creatinine either failed to occur or their retention was slight in comparison with the retention obtained in the same animal from the initial uranium intoxication.

MAGEE, H. E. and J. J. R. MACLEOD (ABERDEEN, SCOTLAND). Diffusion through the Walls of Surviving Intestine.

Solutions of substances such as acids, potassium iodide and the sugars, when placed in loops of living intestine immersed in Tyrode's solution, diffuse out more slowly than through intestine that has been killed by heat or by sodium fluoride. Although this difference in diffusibility may depend to some extent on a change in the physical structure of the gut wall, due to coagulation of protein, the possibility exists that the function of selective absorption of the living mucosa could be demonstrated and its properties investigated by this method. To test this possibility the following experiments have been performed, using in all cases neighbouring pieces of rabbit intestine: (1) the rates of diffusion of equimolecular solutions of various pentoses and hexoses. It was found, in general, that the hexoses diffused much more rapidly than the pentoses. The following results, which give the percentage of sugar diffused out in the times indicated, will exemplify:

	25 MIN- UTES	50 MIN- UTES	75 MIN- UTES	90 MIN- UTES	115 MIN- UTES
M/2 Glucose, gm. sugar per cent.....	0.016	0.047	0.076	0.110	0.130
M/2 Xylose.....	0.008	0.026	0.040	0.053	0.065

(2) The rates of diffusion of the same substances at varying temperatures. Between the temperatures of 3°C. and 10°C. the increase in rate of diffusion of dihydroxy acetone was 72 per cent for dead intestine and 35 per cent for living; between 25 and 39° in the same experiment the increase in rate of diffusion for the dead intestine was 30 per cent and for the living 112 per cent. (3) The relation between rates of diffusion and the concentration of the solution. Within certain limits, the rate of diffusion is much less dependent on the concentration in living than it is in dead intestine. Thus, the following amounts of KI diffused in the same time through the walls of adjacent living and dead segments of intestine, into which equal quantities of 0.15, 0.175 and 0.2 per cent solutions had been placed: living 20, 20 and 37γ; dead 22, 34, and 55γ for the solutions in order of increasing concentration (1 γ = 0.0000001 gm.). The method also offers a means for investigating the action of such enzymes as the invertases. Thus, practically no cane sugar was found to diffuse out when the intestine was living (although invert sugar diffused) but diffusion occurred rapidly when it was killed. Various other agencies, besides heat and sodium fluoride, have been used to kill the intestine (KCN, exposure to air, etc.). In every case these have given similar results.

MAIGNON, F. (PARIS). **Caractères de l'acidose physiologique chez le chien—Influence de l'administration de bicarbonate de soude sur le métabolisme cétonique chez les diabétiques soumis au régime gras et chez le chien en état d'acidose physiologique.**

F. Maignon a montré en 1908, sur une chienne diabétique, que le régime gras entraîne rapidement la disparition du sucre, de la dénutrition azotée, avec relèvement de l'état général et que l'acétonurie diminue au lieu d'augmenter si l'on a le soin de ramener l'acidité urinaire à la normale par l'administration de bicarbonate de soude.

Ces résultats cliniques furent confirmés par Karl Petren de Lund, à partir de 1913, au cours d'une expérimentation clinique de plus de dix années et par Newburgh et Marsh à partir de 1918.

F. Maignon et L. Morand montrèrent en 1913, sur le chien, que la viande est beaucoup plus cétogène que la graisse.

F. Maignon et E. Knithakis ont étudié en 1926-28 l'acidose physiologique chez le chien et l'influence, sur la cétose, de l'administration de bicarbonate de soude, en quantité juste suffisante pour ramener l'acidité urinaire à la normale.

Les conclusions sont les suivantes:

—La diète hydrique et le régime adipocarné diminuent fortement le volume d'urine chez le chien alimenté au préalable à la soupe de pain.

—Contrairement à ce qui se passe chez l'homme, l'acidose du jeûne chez le chien n'est généralement pas compensée, il y a abaissement du pH avec maintien de la réserve alcaline dans les limites normales. Il n'existe pas de cétose. L'acétone urinaire augmente un peu par litre et par 24 heures mais l'acide β oxybutyrique, qui augmente par litre, diminue souvent de moitié par 24 heures. L'administration de bicarbonate de soude, qui accroît un peu le volume d'urine, diminue l'élimination de l'acétone et de l'acide β oxybutyrique, à la fois par litre et par 24 heures.

Mêmes résultats dans le régime adipocarné.

Le fait de ramener l'acidité urinaire à la normale, par l'administration de bicarbonate de soude, a donc pour résultat, dans les cas précités, de diminuer la production des corps cétoniques par une action sur le métabolisme.

MAIGNON, F. et A. PAINVIN (PARIS). **Influence des saisons sur les combustions respiratoires chez le chien.**

De 1904 à 1913 F. Maignon a montré, l'existence d'une influence des saisons et des glandes génitales sur le glycogène musculaire chez le chien, le cobaye, le pigeon et la carpe, sur la sensibilité de l'organisme à l'intoxication protéique chez le rat et sur les combustions respiratoires chez le cobaye alimenté. Les courbes de variations présentent toujours un maximum au printemps, très souvent un second, moins important, à l'automne, et deux minima, l'un en été, l'autre en hiver.

En 1927-28 F. Maignon et A. Painvin ont étudié l'influence des saisons sur les combustions chez le chien, à la fois chez des sujets à jeun (métabolisme basal) et sur les mêmes sujets alimentés à la viande, à raison de 40 gr de viande cuite par Kg de poids vif. La différence entre les chiffres, à une même époque, donnait l'action dynamique spécifique de la viande au moment considéré. Les animaux étaient maintenus en hiver dans des locaux chauffés, de façon à annihiler le plus possible le facteur thermi-

que. Les combustions étaient déterminées par la méthode de confinement, en plaçant les sujets pendant 14 à 15 heures dans une cage respiratoire de 2 mc.

Ces recherches ont montré que la consommation d'oxygène, chez l'animal à jeun et au repos (métabolisme basal), passe par deux maxima au printemps et à l'automne, et par deux minima, l'un en hiver, l'autre en été. Le maximum de printemps est plus élevé que celui d'automne. Certaines années, les maxima sont beaucoup plus marqués que d'autres. F. Maignon avait fait la même constatation à propos du glycogène musculaire.

Les courbes de variations de l'animal alimenté à la viande ne sont pas exactement parallèles à celles de l'animal à jeun. L'écart (action dynamique spécifique) paraît réduit à l'époque des maxima du printemps et de l'automne, surtout lorsque ceux-ci sont accentués.

MALMOS, HAGVIN (LUND). **Lundgren's Angle-Centrifuge. (Demonstration)**

MAMMOSER, L. F., R. W. ALBI and T. E. BOYD (CHICAGO). **Studies on the Absorption of Histamine from the Intestine.**

Several authors have described pathological changes in the stomach and intestine of the dog following removal of the parathyroids. Spadolini has argued that the mucosa is rendered more permeable, and that parathyroid tetany is caused by an increased rate of absorption of toxic substances, derived from bacterial action on proteins. He reports that symptoms, comparable to tetany, are produced from treatment of the mucosa with a solution of chloroform in oil, and considers that these effects are similarly due to absorption of toxic substances through the damaged mucosa. There has been little direct evidence, however, of such a change in permeability toward any specific chemical body found in the intestine.

Using dogs under barbital or ether anesthesia, we put into the duodenum or colon 5 mgm. of histamine dichloride per kilo body weight. In normal dogs the blood pressure is not affected. We obtained similar negative results with dogs which had been parathyroidectomized 6 to 8 days previously. In normal dogs, however, when any of the following agents had been put into the gut, the subsequent introduction of histamine caused a prompt and prolonged fall of blood pressure:

Chloroform, diluted with 1 to 2 volumes of paraffin oil.

Ethyl alcohol, 15 to 30 per cent concentration.

Carbon tetrachloride, undiluted.

HCl, 0.4 per cent.

Dog's gastric juice, of free acidity equivalent to 0.4 per cent HCl, seemed less effective than the pure acid. Doubtful results were obtained with dilute mustard oil and with sodium fluoride solutions.

We conclude that the permeability of the intestinal mucosa toward histamine is increased by the chemical agents named above, but not by loss of the parathyroids.

The gastro-intestinal tract in the parathyroidectomized animals showed no macroscopic change from the normal. Histologic examination was not made.

MANN, FRANK C., JESSE L. BOLLMAN and J. MARKOWITZ (ROCHESTER, MINNESOTA). **A Study of the Relation of the Liver to the Process of Coagulation of the Blood.**

The data that have accumulated bearing on the relation of the liver to the process of coagulation of the blood are summarized. These data are based: 1, on observations of the coagulation time before and after removal of the liver; 2, on regeneration of fibrinogen after defibrination in normal and dehepatized animals; 3, on the effect of anticoagulants in normal and dehepatized animals, and 4, on the heart-lung-liver preparation. The coagulation time of the blood following complete removal of the liver is variable. In some cases the dehepatized animals have reacted in a manner similar to normal animals; that is, the blood coagulates more rapidly after operation, and the coagulation time may not increase for more than twenty-four hours after removal of the liver. In other hepatectomized animals coagulation has been delayed immediately following removal of the liver, but has been normal at later periods. Other animals have shown a progressive increase in coagulation time up to complete failure of coagulation.

It would appear that the delay in coagulation time of the blood in these animals is due to deficiencies in the fibrinogen of the blood, although a simple relationship does not appear between fibrinogen content and coagulation time. The regeneration of fibrinogen appears to be absent following the defibrination of the blood in hepatectomized dogs, in contrast to the rapid regeneration of fibrinogen in similarly treated control animals, although here again exceptions have been noted. Some preliminary experiments indicate that peptone may produce its usual effect on coagulation after removal of the liver, and that rattlesnake venom may be without effect on the coagulation of the blood in dehepatized animals.

MANSFELD, G. (PÉCS). **Über die dynamische und energetische Bedeutung der Herzerweiterung (mit kinematographischer Demonstration der Herzerweiterung am Herz-Lungen Präparat).**

Es kann—wie durch Ausschalten der Sinusgegend am Froschherzen—durch Formalin-oder Phenolpinselung der Vena cava superior am Hundherzen, in wenigen Minuten eine mächtige Dilatatio cordis hervorgerufen werden, welche—wie quantitative Untersuchungen am Herz-Lungen Präparat zeigten weitgehend unabhängig ist von Pulszahl und Schlagvolum.

Aus diesen Versuchen wird gefolgert, dass in der Sinusgegend Apparate vorhanden sind, deren Ausschaltung mit einem Verlust des Herztonus einhergeht.

Diese Erkenntnis ermöglichte die Bedeutung der Herzerweiterung sowohl für die Dynamik, als auch für die Energetik der Herztätigkeit quantitativ zu prüfen. Dabei zeigte sich, dass die Leistungsfähigkeit des erweiterten Herzen im akuten Versuch keineswegs geringer ist als die des normalen, nur verschwindet die Proportion zwischen Arbeitsgrösse und Herzvolum, so, dass kleinste und grösste Arbeit mit fast gleichem Volum ausgeführt wird.

Bezüglich der energetischen Verhältnisse zeigte sich, dass das dilatierte Herz gleich grosse Arbeit ökonomischer leistet als das normale. Wenn also die Herzerweiterung in der Tat ein kompensatorischer Vorgang ist, so liegt die Bedeutung dieser Kompensation darin, dass die Arbeit mit besserem Nutzeffekt ausgeführt wird.

MANSFELD, G. und A. LANCZOS (Pécs). Erregbarkeit und wirkliche Erregungsgrösse des Nerven und die Ungültigkeit des Alles oder Nichts Gesetzes der Erregung.

Wird eine Nervenstrecke narkotisiert, so sinkt bekanntlich die elektrische Erregbarkeit der narkotisierten Strecke, woraus auf eine verminderte Funktion gefolgert wird. Misst man die Erregungsgrösse an der Muskelzuckung, so findet man, dass jene Stromstärke die sämtliche Fasern trifft—also vor der Narkose maximal wirkte—vom narkotisierten Teil eine geringere Zuckung hervorbringt. Dies ist im Sinne der dekrementlosen Nervenleitung nur so zu deuten, dass nicht die Erregung vermindert ist (denn diese müsste ja im unversehrten peripheren Teil wieder zur ursprünglichen Höhe anschwellen) sondern dass jetzt trotz maximaler Stromstärke nicht alle Fasern erregt wurden, dass also der Reizstrom im narkotisierten Nerven, offenbar durch Zunahme des Widerstandes eine Abschwächung erfuhr, was die verminderte Funktion vortäuschte. Dann ist aber der, vom narkotisierten Teil abgeleitete Aktionsstrom auch kein Mass für die wirkliche Erregungsgrösse, denn der grössere Widerstand leistet dem austretenden Aktionsstrom ebenso ein Hindernis als dem eintretenden Reizstrom. Die wirkliche Erregungsgrösse musste also mit mechanischen Reizen geprüft werden. Dabei ergab sich folgendes:

1. Bei geringer Narkot. Konzentration, wenn die elektr. Erregbarkeit der narkotisierten Strecke schon wesentlich geringer ist als jene des unversehrten zentralen Nervenastes, löst maximale mechanische Reizung (Durchschneidung) vom narkotisierten und vom unversehrten Nervenast gleich grosse u. zw. maximale Zuckungen aus.

2. Bei höheren Konzentrationen erfolgt vorübergehend ein Stadium in welchem maximale mechanische Reizung der narkotischen Strecke weit geringere Zuckung auslöst als gleiche Reizung zentral oder peripher.

Dies beweist, dass eine geringere Erregung unverändert als solche zum Muskel gelangen kann und in der unversehrten peripheren Strecke nicht wie man im Sinne der dekrementlosen Erregungsleitung annimmt zur ursprünglichen Höhe anschwillt. Somit ist das A.-o.-N.-Gesetz der Erregung für den Nerven ungültig, denn eine verminderte Erregung kann auch im unversehrten Nerven eine geringere Erregung wecken.

MARGARIA, R. e C. TALENTI (TORINO). Gli equilibri fisico-chimici del sangue nell'aria rarefatta.

Dimostrazione di nomogrammi alla d'Ocagne, illustranti i principali equilibri fisico-chimici del sangue secondo Henderson, eseguiti comparativamente in animali a pressione barometrica normale ed a pressione barometrica ridotta.

MARSHALL, E. K., JR. (BALTIMORE). The Secretion of Urine by the Aglomerular Kidney.

This is an extension of work already reported on the goosfish, *Lophius piscatorius* (Marshall and Grafflin, Johns Hopkins Hosp. Bull., 1928, xliii, 205). The toadfish, *Opsanus tau*, was found to have an aglomerular kidney. In these two fish with purely tubular kidneys, the composition of the urine is found to be essentially the same as that of fish with glomerular kidneys. The threshold phenomena shown by the glomerular kidney is

exhibited by the purely tubular kidney: chloride and phosphate may disappear from the urine under some conditions and under others may be present in large amounts. The aglomerular kidney of fish differs from the glomerular one in showing a specificity (similar to that exhibited by the salivary gland, liver, and pancreas) in the elimination of substances not normally present in the urine. Thus, phenol red is readily excreted in concentrated form by the aglomerular kidney, while sodium carminate, ferrocyanide and glucose are not excreted. All of these substances are eliminated by the glomerular kidney. The excretory function of the tubule would appear to be of a kind similar to that exhibited by secretory glands such as the liver, pancreas and salivary glands.

MARTINO, G. (MESSINA). Sul determinismo della glicemia digestiva.

L'A. in base a personali ricerche sperimentali ha richiamato l'attenzione su una particolare sostanza iperglicemizzante, che il pancreas normalmente elabora, e che si può estrarre sia dall'organo, sia dal secreto che il medesimo versa nell'intestino. Durante il digiuno si accumula nel pancreas, e subito dopo si versa più abbondantemente nell'intestino, in cui risulta assorbibile.

L'azione di tale sostanza sul tasso glicemico interviene nel determinismo della nota iperglicemia da ingestione di sostanze proteiche, o più generalmente da sostanze atte a eccitare la secrezione gastrica, e conseguentemente poi anche quella pancreatica. Infatti, somministrando sostanze proteiche a cani operati di legatura del dotto pancreatico o di fistola pancreatica permanente (in condizioni cioè di impedito passaggio della sostanza iperglicemizzante nello intestino), l'iperglicemia digestiva manca, e si osserva anzi diminuzione del contenuto in glicosio del sangue. Questa ipoglicemia si evita associando alla legatura del dotto pancreatico quella delle vene pancreatiche, nelle quali condizioni la somministrazione di sostanze proteiche non provoca nessuna variazione del tasso glicemico. Nei cani operati di legatura delle sole vene pancreatiche la somministrazione di sostanze proteiche determina una iperglicemia molto più forte che negli stessi animali prima dell'operazione.

L'A. ritiene pertanto che il pancreas durante il periodo digestivo regoli il tasso glicemico con due meccanismi antagonisti, cioè da un lato con una maggiore immissione di insulina nel torrente circolatorio, e dall'altro versando nell'intestino la sostanza iperglicemizzante, che, assorbita, partecipa alla glicoregolazione. Quando manca l'azione di una delle due sostanze prevale quella dell'altra e quindi si osserva, a seconda dei casi, o una maggiore iperglicemia, o invece l'abbassamento del tasso glicemico.

MATTILL, H. A. and H. I. MATTILL (IOWA CITY). Further Studies of Anti-Oxidants.

The effectiveness of hydroxyl derivatives of benzol in prolonging the induction period of auto-oxidizable animal fats depends upon the number and location of the hydroxyl groups. When these are in the ortho or para positions one milligram of the substance in ten grams of lard at 70°C. prevents the uptake of oxygen for weeks while when in the meta position the oxidative process is not delayed. Pyrogallol is effective, inositol is not. Acetylation destroys the anti-oxidizing capacity. In the naphthalenes one hydroxyl group is sufficient if in the α position; β -naphthol is ineffective.

The anti-oxidants in vegetable oils occur in the unsaponifiable portion not precipitable by digitonin. Cholesterol, sitosterol, and various vitamin concentrates such as oscodal, acterol and ergosterol have no anti-oxidizing action. The results of simultaneous feeding tests on rats suggest that while vitamin E may not be merely an anti-oxidant, the presence of anti-oxidants protects it from destruction by the peroxides naturally occurring in animal fats or developed in them by manipulation. The well-recognized protection afforded to vitamin A by anti-oxidants such as hydroquinone and wheat germ oil, if operative within the body as well as outside, provides another explanation for the suggested occurrence of vitamin A in wheat germ oil.

MAYERSON, H. S. and HENRY LAURENS (NEW ORLEANS). **The Ineffectiveness of Radiant Energy on Hemorrhagic Anemia in Dogs.**

Employing the procedure and diet elaborated by Whipple and his associates, anemia was produced in 19 dogs. Carbon arc irradiation produces marked and persistent increases in the number of erythrocytes and reticulocytes. The red cells are smaller than normal but the saturation index, that is to say, the ratio of the color index to the volume index, which is the same thing as the Hb percentage divided by the volume percentage, has the usual or normal value. Massive exposures given at long intervals are usually more effective in evoking these responses than are smaller doses repeated more often. An increase in Hb was noted in only one experiment where a single massive carbon arc exposure was followed by the production of 23.5 grams over and above the amount formed in a similar two-week control period. A second exposure was ineffective. In ten cases the amount of Hb formed during and immediately following the irradiation period is less than in the previous, or later, control periods. In the remaining eight cases carbon arc radiation had no effect on the Hb. The absence in such radiation of any marked stimulus to Hb formation is further shown by the fact that dried peaches or apricots added to the diet of animals which have shown no response to radiation produce typical acceleration of Hb formation, and this is not demonstrably influenced by any dosage of radiant energy, although the changes in reticulocytes and erythrocytes which characteristically follow carbon arc irradiation are now absent. Irradiation of six dogs with the quartz mercury vapor arc gave similar negative results.

McCLENDON, J. F., CLAIRE CONKLIN, FRANK WILDEBUSH and HAROLD WILES (MINNEAPOLIS). **The Ovarian Hormone in Relation to Women.**

From biometric analysis of 438 determinations of basal metabolism on ten women, including the calculation of the probable errors, it was shown that the basal metabolism rises during the pre-menstrual period and falls during menstruation to the lowest level during the post-menstrual period. The excretion of the ovarian hormone follows the same curve. During menstruation no ovarian hormone could be determined in the urine. During the post-menstrual period 12 single-injection mouse units were recovered from a 24 hour specimen of urine. During the pre-menstrual period 48 single-injection mouse units were recovered from a 24 hour specimen of urine. Twenty-four mouse units were present in 12 cc. of the blood plasma at the beginning of the inter-menstrual period and 126 units at

the end. None was found in the corpuscles. Owing to the positive correlation between the hormone and the basal metabolism an attempt was made to raise the basal metabolism by injecting the hormone. It was found that the single-injection doses up to about 4000 mouse units at 8:00 a.m. was followed by a very slight rise in the metabolism to 6:00 p.m. but owing to the necessity of withholding food, the metabolisms were interrupted. At 8:00 a.m. the next day there was a normal basal metabolism. The metabolism of the same subjects without injection of hormone rose slightly during the day but not as much as with injection. By giving several injections a day it was possible to raise the metabolism still higher and also caused an increase in metabolism the following day.

Women who had never menstruated showed none of the hormone in their blood. Injections of hormone were made into women who had never menstruated and who were undeveloped in secondary sexual characters and accurate measurements of the secondary sexual characters were made. One of these, 20 years old, reported menstruation following injections. In women who had menstruated but at the time had had amenorrhea of considerable duration, injection of the hormone caused menstruation to occur again.

It was found that the ovarian hormone could be extracted from the urine of women in late pregnancy not only by ether but by carbon tetrachloride. The hormone could be adsorbed from the urine on cellulose pulp or on freshly precipitated calcium phosphate. From one liter of urine 100 "3-injection" mouse units were adsorbed to cellulose pulp and extracted therefrom with alcohol. From another liter of urine 265 "3-injection" mouse units were adsorbed to calcium phosphate and recovered by dissolving the phosphate in acid.

McGINTY, DANIEL A. (ANN ARBOR). **The Carbon Dioxide Content of the Brain of the Frog under Varying Conditions.**

The intact frog (*R. pipiens*) was subjected to CO₂ tensions ranging from 0 to 200 mm. in room air, in low oxygen (3-3½ per cent) and in high oxygen (75-100 per cent) for periods of ½ to 2½ hours. The brain was quickly removed in a chamber containing the same gas as administered to the frog, carefully avoiding rupture of the endolymphatic sac, and placed in a tared capsule containing sufficient glycerol to cover the tissue. Total CO₂ content was determined by the electrical conductivity method of Fenn.

The CO₂ content of frog brain at 0 mm. CO₂ tension in room air was 23 vols. per cent and rapidly increased to 62 vols. per cent at 100 mm. and to 74 vols. per cent at 200 mm. The CO₂ content in low O₂ at 0 mm. CO₂ pressure averaged 16 vols. per cent and approximately equalled the CO₂ content of brain in room air at 100 and 200 mm. CO₂ tensions. In high O₂ the CO₂ level at 0 mm. tension was 26 vols. per cent. At 100 and 200 mm. the CO₂ content followed the room air curve at a slightly higher level.

The diminished CO₂ content at the lower pressures of CO₂ in low O₂ may be due not only to decreased tissue buffers as a result of organic acid formation but to increased lung ventilation which seemed to prevail. The similar height of the curves at the higher tensions of CO₂ whether in low O₂ or in room air may result from equally depressed oxidations due to CO₂ itself (Gesell, 1928). The higher level of the CO₂ curve at the higher

pressures of CO₂ and O₂ may be indicative of the beneficial effects of high O₂ pressures.

McSWINEY, B. A. and J. M. ROBSON (LEEDS). Reaction of Smooth Muscle to Stimulation of the Vagus and Sympathetic Nerves in Isolated Nerve Muscle Preparations.

Isolated preparations of mammalian smooth muscle supplied by the vagus and sympathetic nerves have been made. These preparations have enabled us to examine the responses of the muscle to stimulation of the nerve fibres.

Stimulation of the vagus nerve with a single break shock evokes a contraction. The record demonstrates a latent period of 0.5 second period of contraction 1.5 seconds, and relaxation 10 seconds. On stimulation with a faradic current, a greater contraction was obtained than with a single break shock. Two break shocks were also found to increase the height of contraction if separated by an interval greater than 0.005 second.

Contraction of the muscle was recorded on stimulation of the vagus nerve in practically all experiments. Variations in the frequency or strength of the current did not alter the response, but, after addition of atropine, relaxation was obtained on stimulation of the nerve.

On stimulation of the sympathetic nerve supplying strips of muscle from adjoining regions of the stomach, a contraction or relaxation of the muscle was recorded; if the muscle relaxed on stimulation of the nerve with a high faradic current, contraction was obtained on decreasing the strength or frequency of the current, but, if contraction was first recorded, alteration in the frequency or strength of the current did not affect the response. Ergotoxine abolishes the motor response.

MEYERHOF, OTTO, DEAN BURK und KEN IWASAKI (BERLIN-DAHLEM).

Ueber die Fixation des Luftstickstoffs durch Azotobakter.

Analyse der Faktoren, welche den Umfang der Stickstoffxation und das Verhältnis derselben zur Atmung d.h. die Energie ausbeute der Sauerstoffatmung bedingen: Grösse und Konstanz des Sauerstoffdrucks, Konzentration an Huminsubstanzen, Alter und Wachstumsperiode der Kultur. Unter geeigneten Umständen lässt sich das Teilungsstadium und das Fixationsstadium der Bakterien zeitlich vollständig voneinander trennen.

MICHAELIS, L. (BALTIMORE). Complex Compounds of Cysteine with the Metals of the Iron Group.

According to Warburg, oxidation of cysteine by oxygen takes place only by the action of some metal salts as catalysts, especially iron. It is desirable, therefore, to make a comparative study of the complex compounds of cysteine with the metals of the iron group, Ni, Co, Fe, among which only Fe works as catalyst. Ni salts give at pH 7-8 a very stable soluble bordeaux red complex with cysteine, which is not altered by the presence of oxygen. Co gives at pH 7-8 in complete absence of oxygen with cysteine a soluble cobaltous complex of relatively faint color, olive green, when the ratio of Co to cysteine is about 1:2 or 1:3, pink when cysteine is in large excess. This cobaltous cysteine is one of the most powerful reductants. It rapidly absorbs oxygen from the air, it reduces all reversible organic dyestuffs immediately, even phenosafranin, it shows a reduction potential matching under certain conditions that of the

hydrogen electrode at the same pH. The oxidation product is deep brown. The amount of oxygen consumed is maximum when the ratio of cobalt atoms to cysteine is 1:3, and 1 atom of oxygen is consumed, *i.e.*, twice what would be necessary to oxidize the cobaltous state to the cobaltic. The amount of oxidant consumed as to show a potentiometric endpoint of the oxidation is equivalent to the amount of oxygen consumed. When the oxidation is performed with ferricyanide, two steps of oxidation can be recognized potentiometrically. Cobaltous cysteine in absence of oxygen gives also with cystine a brown complex, which is less intensely colored than the one obtained by ordinary oxidants or oxygen. The fully oxidized cobalt complex is a very stable compound. Iron gives at pH 7-8 a practically colorless soluble ferrous cysteine complex, which is oxidized by air or dyestuffs to the violet complex, which gradually fades out, giving rise to cystine and ferrous iron. The instability of the oxidized iron complex involves the catalytic effect of iron as Warburg has already shown. The difference between iron and cobalt, therefore, is that the oxidized cobalt complex is stable. This deprives cobalt of the catalytic property and permits studying the oxidized metal complex, which is unaccessible for an analysis in the case of iron because of its lability. With sufficient criticism the oxidized cobalt complex or one of the steps of oxidation of the cobaltous complex may serve as a model for the labile oxidized iron complex, and may lead to a fuller understanding of the chemistry of the iron catalysis.

MILES, WALTER R. (STANFORD UNIVERSITY, CALIFORNIA). **Drug Effects Measured by Acquired Patterns of Response.** (Cinematograph demonstration)

In addition to experimenting with drugs on muscles, other separate body systems, and isolated organs, it is desirable to study drug influence on the total animal. For this purpose locomotion, feeding, fighting, and sex play have been used, but it is difficult to get quantitative results on these because the natural action patterns are variable. A second difficulty is the frequent inability to elicit these native responses with certainty; for instance, the rat may climb when we want him to feed. Acquired behavior is much more susceptible to temporal control. The conditioned reflex could be used for our purpose; however, a series of actions offers a better chance for observation.

Rats easily learn the path to their food on a complex elevated skeleton maze with many turns and opportunities for errors. Their progress can be watched without distracting their attention. The posture, motor coördination, errors, retracings, and time may be recorded. A group of thirty animals after twenty days of special maze training constitutes an excellent agency for comparing the effects of injected substances.

Results are reported on morphine, strychnine, caffeine, cocaine, hyoscyne and alcohol. Introduction was by intraperitoneal injection and minimal doses were used. Alcohol caused incoördination in locomotion and balance but no loss of orientation or memory. In contrast to this, hyoscyne caused the animals to explore as if on the maze for the first time; memory was much disturbed but coördination was normal. No drug yet tried has been found to produce a performance which is an improvement on the normal. Typical results are shown by motion pictures.

MILLER, FREDERICK R. (LONDON, ONTARIO). **Combined Head-Holder and Clamp for Decerebration of Mammals. (Demonstration)**

MILLS, C. A. (CINCINNATI). **Rhythmic Alternation of Visual Function in Our Two Eyes. (Demonstration)**

The alternation of visual function in the two eyes is of a continued rhythmic character and resists efforts at control by attempts to fix the attention. This is not a phenomenon of retinal fatigue, since vision in the non-functioning eye returns almost at once when to the other eye is presented a blank white surface. To call the alternation retinal rivalry seems unwarranted, as well as to say that it is *due* to alternation of attention.

MODRAKOWSKI, G. et R. LENTZ (VARSOVIE). **Recherches sur l'acidose et l'alcalose artificielles. I. Sédimentation des globules rouges, variations de concentration du plasma et du sérum et de la perméabilité des capillaires sous l'influence des perturbations de l'équilibre acide-base.**

Dans l'acidose artificielle provoquée chez l'homme par l'absorption de 15 à 25 gr. NH_4Cl et chez le lapin par 1 gr. par kilog, nous avons observé une sédimentation beaucoup plus rapide des globules rouges (méthode de Linzenmeyer), une concentration très prononcée du sang, mesurée par l'index réfractométrique du plasma hirudinisé et du sérum. Si l'on pose la différence comme l'expression du fibrinogène, on trouve que la relation entre les divers constituants protéiques du sang ne change point. La perméabilité des vaisseaux capillaires, examinée par la méthode de l'emplâtre de cantharide, augmente. L'ampoule se produit dans un laps de temps plus court qu'à l'ordinaire, et le contenu du liquide en albumine est plus grand.

Le résultat est que l'index de la perméabilité, d'après Petersen, c'est-à-dire la relation entre le pourcentage d'albumine du sérum et de l'exsudat s'élève.

L'alcalose provoquée par 30 à 40 gr. NaHCO_3 chez l'homme et chez le lapin, par environ 2 gr. NaHCO_3 par kilog ou 0.3 à 0.8 NaOH , donne des résultats opposés: ralentissement très prononcé de la sédimentation des globules rouges, dilution du sang, mais avec cela une augmentation souvent très considérable du taux du fibrinogène et diminution de la réaction inflammatoire par l'emplâtre de cantharide. L'ampoule se forme plus lentement et contient moins d'albumine. Donc l'index de la perméabilité s'abaisse.

Mais il faut se rendre compte que l'alcalose bicarbonique en vérité ne dure que peu de temps et que ce n'est pas une alcalose pure, puisque l'acide carbonique se dégageant de NaHCO_3 dans l'organisme, agit dans le sens de l'acidose gazeuse. Pour cette raison l'exsudation sous l'action de l'emplâtre de cantharide étant très ralentie pendant la phase alcalique ou même complètement empêchée, peut se former plus tard quand déjà la phase alcalique décline; alors le contenu de l'exsudat en albumine peut augmenter et, en ce cas, l'index de perméabilité pourrait se rapprocher du chiffre de celui de l'acidose.

Dans l'alcalose obtenue par la soude caustique, qui serait la véritable alcalose, on n'observe jamais d'élévation de l'index de perméabilité qui est toujours très bas.

Sous l'action de NaOH on reconnaît chez le lapin tous les symptômes

théoriquement exigés pour l'alcalose, notamment une respiration très ralentie et plus superficielle. Pendant l'alcalose bicarbonique, la respiration, comme on le sait bien, ressemble plutôt à celle de l'acidose.

Comme illustration nous présentons 3 expériences sur des lapins.

TABLEAU

	% ALB. PLASMA	% ALB. SÉRUM	% FIBRINOGENE	% ALB. EXSUDAT	INDEX DEFERMÉAT	FORMATION DE L'AMPOULE EN-HEURES	SÉDIMENTATION DES GLOBULES ROUGES (HEURES)
1. Lapin pesant 2080 gr.:							
Norme.....	6,85	6,30	0,55	3,57	60	14 h.	Pas mesurée
Acidose par 2 gr. NH_4Cl	8,27	7,66	0,61	5,32	68	12 h.	2 h. 30
2. Lapin pesant 1700 gr.:							
Norme.....	7,53	6,89	0,64	4,57	66	12 h.	Pas mesurée
Alcalose par 4 gr. NaHCO_3	7,25	6,40	0,85	4,55	70	17 h.	20 h.
3. Lapin pesant 2860 gr.:							
Norme.....	6,57	6,01	0,56	4,75	79	13 h.	Pas mesurée
Alcalose par 0.86 gr. NaOH	5,43	4,35	1,08	0	0	L'ampoule ne s'est pas formée	Plus de 24h.

Sur des sujets humains nous avons obtenu des résultats tout à fait concordants. Nous ne citons que les différences de vitesse de la sédimentation des globules rouges qui étaient de 6 à 10 heures pendant la norme, de 3 à 6 heures pendant l'acidose et de plus de 24 heures pendant l'alcalose.

Chez l'homme nous avons examiné en outre le pH du sang et du contenu de l'ampoule de cantharide avec l'électrode de quinhydrone. Tels sont les résultats obtenus pendant la norme, l'acidose et l'alcalose sur un même sujet:

Dans la norme le pH du sang était 7,413, et le pH de l'exsudat: 7,185; après le traitement alcalique de 5 jours à 40 gr. de NaHCO_3 par jour: pH du sang 7,423, de l'exsudat 7,277; après 5 jours d'acidose à 20 gr. de NH_4Cl par jour: pH du sang 7,255, pH de l'exsudat 7,068.

MONJE, MANFRED (ROSTOCK). Die gegenseitige Beeinflussung der durch zwei kurzdauernde Lichtreize hervorgerufenen Empfindungen.

Es wurde die Wirkung zweier kurzdauernder Lichtreize untersucht, die sich in solchem Intervall folgen, dass noch keine Verschmelzung eintritt. Führt man am fixierten Auge einen Lichtspalt vorüber, so lassen sich an der dem Spalt entsprechenden Empfindung folgende Einzelheiten untersuchen: 1. die Zeit, welche vergeht zwischen der Einwirkung des Reizes und dem Eintritt der Empfindung, die Empfindungszeit; 2. die Dauer der Empfindung, die in der Breite des dem Spalt entsprechenden Lichtstreifens zum Ausdruck kommt; und endlich die Helligkeit bzw. deren Verteilung in dem Lichtstreifen. Folgen zwei gleichhelle Lichtreize einander, so lassen

sich gegenseitige Beeinflussungen der Empfindungen feststellen, abhängig von der Intensität und dem zeitlichen Abstand der beiden Spalte. Der stärksten Beeinflussung unterliegt die Dauer der zweiten Empfindung: sie wird verlängert. Die Dauer der ersten Empfindung wird ebenfalls verlängert, sowie eine Wirkung des zerstreuten Lichtes des zweiten Spaltes möglich ist, jedoch in geringerem Masse. Hervorzuheben ist das bei gleichbleibendem zeitlichen Abstand der Lichtreize beobachtete Verhalten der Empfindungszeit des zweiten Spaltes: sie wird bei starken Intensitäten vergrößert, bei schwachen verkleinert. Eine Beeinflussung der Empfindungszeit des ersten Lichtreizes war nicht nachweisbar. Ebenso liessen sich Veränderungen der Helligkeit nicht mit Sicherheit feststellen. Dagegen ist häufig ein Helligkeitsmaximum zu beobachten, das bei Verkürzung der Empfindungszeit der zweiten Empfindung in einem früheren Abschnitt liegt und dadurch einen steileren Helligkeitsanstieg bedingt. Bei starken Reizen konnte zunächst in der zweiten, bei sehr starken auch in der ersten Empfindung die Andeutung eines dunkeln Intervalles beobachtet werden, eine Beobachtung, die zu der Erscheinung der Nachbildphasen bzw. der Phasenvermehrung überleitet. Bemerkenswert ist, dass die den Spalten entsprechenden Lichtstreifen umso näher aneinander zu rücken scheinen, je grösser ihre Geschwindigkeit ist, ein Verhalten, das als Verdichtung bezeichnet wird und in erster Linie auf der Verkürzung des zeitlichen Intervalles zwischen den Reizen beruht.

MONTGOMERY, M. LAURENCE and THOMAS H. LIFSCOMB (CHICAGO).

A Direct, Continuous Volume Flow Apparatus Utilizing a Modified Ludwig Stromuhr Principle, with the Flow Controlled by a Double Knife Edge, Horizontally Moving Valve Activated by Electrolytically Controlled Solenoids. (Demonstration.)

MOORE, A. R. (EUGENE, OREGON). **The Function of the Fertilization Membrane in the Formation of the Blastula.**

If unfertilized eggs of the sea urchin are exposed for two minutes in an isosmotic solution of non-electrolyte (urea), then fertilized in sea water, they undergo division but without fertilization membranes. Consequently the blastomeres are loosely clumped usually in one layer. The loss of membrane precursor by the egg in the solution of non-electrolyte is irreversible. Na and K ions added to the urea solution do not protect the eggs, but Mg, Ca and Sr ions do. If unfertilized eggs are exposed to a solution made up of $\frac{1}{2}$ cc. of $3/8$ M solution of either $MgCl_2$, $CaCl_2$ or $SrCl_2$ added to 50 cc. of a solution of urea, they will show after fertilization a comparatively inelastic membrane closely investing each egg. This is membrane formation without elevation. The addition to 50 cc. of the urea solution of 2 cc. of a solution of either $MgCl_2$ or $CaCl_2$ results in almost complete protection for the eggs, so after fertilization, the fertilization membrane is formed and elevated as normally. In this reaction Mg ion is equal to Ca ion in protective action, indicating a valence effect. Sr ion is approximately twice as effective as either Mg or Ca, showing a qualitative action in addition to the valence effect. The results prove that membrane formation is of fundamental importance to the development of the metazoa, since without membranes the cells tend to part and cannot form multicellular larvae. The difference between formed membranes and plasma membranes is clear. In cell division without membrane forma-

tion the blastomeres are well rounded and separate, indicating the presence of plasma membranes, but eggs which have previously been treated with a solution of urea + KCl show a weakening of the plasma membranes, and after fertilization give ameboid forms without separation of the blastomeres. Cell bridges between the blastomeres were demonstrated. There are therefore two mechanisms which make the formation of the blastula possible, namely, the membranes and the cell bridges.

MORGULIS, SERGIUS (OMAHA, NEBRASKA). Inactivation of Catalase by Ultra-Violet Radiation.

The inactivation of kidney catalase has been studied at different hydrogen ion concentrations. The inactivation is complete at all pH, but the time required for the complete inactivation varies with the pH of the medium in which the catalase is radiated. The curves of inactivation likewise are very different at different pH values. At pH 6, 7 and 8 the curves of inactivation are straight lines, the loss of activity being proportional to the time of exposure. At all other pH the inactivation of the catalase follows an entirely different course, and is different for each pH. However, they all show the same general behavior in that the inactivation is more rapid during the first few minutes of radiation and slower during the later radiation than in the case of either pH 6, 7, or 8. The minimum inactivation takes place at pH 6.0.

MOSONYI, J. (BUDAPEST). Über das Verhalten des Gehirns normaler, vitaminfrei und vitaminreich ernährter Ratten.

Es wurden Untersuchungen am Gehirne normaler, vitaminfrei und vitaminreich ernährter weisser Ratten angestellt. Die normalen Tiere erhielten eine Nahrung, die aus Brot, wenig Fleisch und Gemüse (Küchenabfälle) bestand. Die vitaminfreie Kost wurde nach Funk, McCollum und Simmonds bereitet. Als vitaminreiche Nahrung diente ein Gemisch obiger vitaminfreier Nahrung und des vitaminhaltigen Präparates "Ovaltine Dr. Wander." Der Vitamingehalt der Ovaltine wurde im Tierversuch (Längewachstum, Gewichtszunahme, erhöhte Vitalität) festgestellt. Nach dem Entbluten aus den Carotiden wurde das Gehirn gewogen und bei 100–120°C. im Trockenschranke bis zur Gewichtskonstanz getrocknet, der Trockengehalt bestimmt, die Trockensubstanz im Mörser fein zerrieben, der Stickstoff nach Kjeldahl und der Phosphor nach Bell-Doisy bestimmt. Es zeigten sich keine auffallenden Unterschiede im Verhältnisse des Gehirns zum Körpergewicht zwischen den normalen und vitaminreich ernährten Ratten; wohl aber zwischen obigen und den bei vitaminfreier Nahrung gehaltenen Tieren, u. zw. in dem Sinne, dass hier die betreffende Verhältniszahl einen höheren Wert hatte. Da der Trockengehalt des Gehirnes vitaminfrei ernährter Tiere normal war, muss angenommen werden, dass bei exper. Avitaminose die Gehirnsubstanz den dissimilatorischen Vorgängen gegenüber eine grössere Resistenz besitzt, als die übrigen Organsubstanzen. Im Trockensubstanzgehalt sind keine Unterschiede vorhanden. Der Stickstoffgehalt des Gehirns vitaminreich (Ovaltine) ernährter Ratten übersteigt beträchtlich den normalen Wert.— Im Phosphorgehalt konnten nur minimale Schwankungen festgestellt werden.

MULDER, A. G. and MAURICE B. VISSCHER (MEMPHIS, TENNESSEE).
The Relation Between Total Metabolism and the Heart Metabolism in Anesthetized Dogs.

The fraction of the total metabolism due to the metabolism of the heart has been determined by measuring the total oxygen consumption of an anesthetized dog and subsequently measuring the metabolism of its heart after isolation in the heart-lung preparation. It has been found that the resting oxygen consumption of the whole animal under chloralose anesthesia is about 450 cc./kgm. body wt./hr., the exact value of course depending on the size of the dog. The lowest observed metabolism of the heart was found to be on the average 2.5 cc./gm. heart. In terms of the body weights of the dogs from which the hearts came, this represents 33 cc./kgm. total body wt./hr. That is to say that the heart metabolism at low levels of heart work represents on the average 7.2 per cent of the metabolism of the whole animal, under the conditions of our experiments, which were nearly basal except for the condition of anesthesia. Upon increasing the work imposed upon the heart the oxygen consumption increases, as previously shown, in proportion to the diastolic ventricular fiber length, and the heart metabolism may reach 8 cc./gm. heart/hr. This represents 100 cc./kgm. total body wt./hr., or more than 20 per cent of the quantity of oxygen consumed by the whole animal at rest.

It is obvious that the heart metabolism represents such a large moiety of the total metabolism of an animal that changes of any magnitude in the former will have very sensible effects upon the latter.

The work is being extended to include a study of the part played by respiratory movements in the sum of body oxygen usages making up the basal metabolic rate.

MULINOS, MICHAEL G. and CHARLES C. LIEB (NEW YORK). **Pharmacology of Learning.**

Dogs and cats were used to study the physiology of the cerebral hemispheres. Salivation induced by pilocarpine does not depend upon conditions other than the actual injection of the drug. Therefore the effector response itself is inadequate to bring about conditioned salivation. Morphine induces salivation and nausea. The salivation is induced by stimuli associated with the administration of the morphine (sight of experimenter). The conditioned salivation is not accompanied by nausea, is more profuse than that produced by morphine itself, and is due to the large number of non-specific stimuli now effective.

Atropine dries the mouth and stimulates the central nervous system. Salivation to conditions previously innocuous is obtained after the repeated administration of atropine. Accordingly, the effector response is unnecessary for the production of reflexes dependent upon the integrity of the cerebrum. These responses can be extinguished by time and training, and they can be reestablished in a fraction of the time previously necessary.

The response to one of several non-specific stimuli may be extinguished by repetition without reinforcement of any, the response to the others being retained. Memory is of two kinds,—*a*, spontaneous: the animal salivates on presentation of the conditioning stimulus; *b*, lack of spontaneous recognition: one reminding application may be sufficient to recondition, even after a lapse of three years. Cerebral alertness is a

balance between these learning-forgetting-remembering (conditioning-unconditioning-reconditioning) processes. A salivary response to the room was extinguished in 8 days, salivation to other non-specific stimuli remaining. Twenty-two days later the dog was again brought into the room and at once salivated. The learning lesson was retained better than the forgetting lesson.

MÜLLER, ERICH A. (DORTMUND). **Über die Energetik der Muskelkontraktion im menschlichen Körper.**

Entwickelt ein Muskel von der Länge l bei maximaler Reizung isometrisch die Spannung P , so hat sich eine messbare Menge chemische Energie E in eine messbare Menge Spannungsenergie R mit dem Wirkungsgrade R/E umgewandelt. Erschlafft der Muskel wieder isometrisch bei der Länge l , so geht die Energie R vollkommen in Wärmeenergie über. Lässt man dagegen den Muskel nach Erreichung der Spannung P sich verkürzen, so geht ein Teil der Energie R in die äussere Arbeit A über. Da man theoretisch die gesamte Energie R ohne Wärmeverlust als Arbeit wieder gewinnt, wenn die Verkürzung dem Längenspannungsdiagramm folgt, bei dem der Muskel bei jeder Länge seine maximale Spannung entwickelt, kann der Wirkungsgrad A/R alle Werte von 0-1 annehmen. Diese von A. V. Hill am Froschsartorius gefundenen Gesetzmässigkeiten konnten wir in Respirationsversuchen am ganzen Menschen mit Hilfe eines besonderen Ergostaten und Ergographen bestätigen. Unsere Untersuchungen ergaben für den Wirkungsgrad A/R bei Verkürzungszeiten von einer Sekunde Werte bis zu 1, wenn die Verkürzung unter einem Spannungsabfall erfolgte, der dem Abfall der Maximalkraft über die Verkürzungsstrecke proportional verlief. Wurde dagegen die gleiche Arbeit isotonisch geleistet, so fanden wir um 40 Procent niedrigere Wirkungsgrade.

MÜLLER, ERICH A. (DORTMUND). **Kohlensäuredichte Atemsäcke. (Demonstration)**

VON MURALT, ALEXANDER L. (ZÜRICH) and JOHN T. EDSALL (BOSTON).

The Double Refraction of Cross-Striated Muscle and of Muscle Globulin.

It has been shown by Stuebel¹ that the double refraction of the anisotropic band of cross-striated muscle is the result of three components. A positive double refraction due to micro-structure ("Formdoppelbrechung"), a positive double refraction of the element of micro-structure itself ("Eigendoppelbrechung") and a small negative double refraction of unknown nature due to the muscle lipoids. The element forming the micro-structure must according to Wiener's theory be a rod shaped particle, small compared with the wave-length of light. Stuebel failed to prove this particle identical with the myosin particles described by Botazzi and Quagliariello.² The indications are however that the particle involved consists of one or more molecules of a protein with an isoelectric point between 6.0-6.6.

A muscle globulin fraction prepared by one of us (Edsall) which has such an isoelectric point, was found to be doubly refracting if the particles

¹ Stuebel. Pflüger's Arch., 1923, cci, 629.

² F. Botazzi and G. Quagliariello. Arch. Int. de Physiol., 1912, xii, 234.

were oriented. The preparation was studied in a rotating apparatus where the orientation is produced by shear. The double refraction appears to be specific for this protein, indicating that it is the main, if not the only constituent of the rod shaped particle in the anisotropic band.

Double refraction in the intact muscle decreases during contraction. The conditions of this effect can be studied on the muscle globulin *in vitro*, if the value of the double refraction in living muscle at rest and in action are known. Accurate measurements have been made on the fibers of the membrana basihyoidea of frog, yielding, as an average 0.0010 for $n_e - n_o$. The mean deviation for different fibres was ± 0.0002 . During a twitch the double refraction has values as low as Stuebel¹ has found in different states of rigor. The measurements were made with the aid of a Sénarmont compensator in connection with a half-shadow method.

MURLIN, JOHN R., HAROLD B. PIERCE and DONALD E. GREGG (ROCHESTER, NEW YORK). **The Relation of the Liver to the Action of Insulin.**

This problem has been studied in three ways: 1, *in vitro*, employing incubation and aseptic technique; 2, perfusion of the liver; and 3, treatment of dogs having pancreatic diabetes. Under the first method attention has been centered on the proportion of true sugar to non-sugar reducing substances with and without the addition of insulin, before incubation, after incubation for from 2 to 24 hours, and after hydrolysis of the remaining glycogen. It has been found that the addition of some organic acids profoundly affects the distribution of the reducing substances as well as the total amounts recoverable after incubation and hydrolysis.

With the second method it has been shown that with proper precautions there is no demonstrable transformation of fat to carbohydrate in the perfused liver. The effect of insulin and adrenalin in the perfusing fluid is being studied as this abstract is written.

With the third method, it has been found that the absorption of insulin from the alimentary tract of the depancreatized dog is materially enhanced by various liver products; as bile, salt solution suspension of liver pulp and some extracts. We are inclined therefore to the belief that the favorable effects of liver pulp on diabetes reported by Blotner and Murphy are due to insulin already present in fresh liver, its absorption being aided in certain individuals by bile or its precursors and possibly by some extractive substances.

MYERS, V. C. and R. F. HANZAL (CLEVELAND). **A Study of Methyl Uric Acids.**

At the last Congress Myers and Wardell² reported a study of the influence of the ingestion of the methylated xanthines, caffeine, theobromine and theophylline on the excretion of uric acid. The possibility was suggested that the apparent increase in uric acid excretion noted after the ingestion of caffeine and theophylline might be due to the excretion of methyl uric acids. It was noted that theobromine did not cause an increase in uric acid excretion and that 3,7-dimethyl uric acid did not give the color reaction.

Through the kindness of Professor Biltz of the University of Breslau we have now had an opportunity to study the color developing properties

¹ H. Stuebel and Tze-Yeh Liang. Chinese Journ. Physiol., 1928, ii, 139.

² V. C. Myers and E. L. Wardell. Skand. Arch. Physiol., 1926, xlix, 189.

and metabolism of all the methyl uric acids of interest in this connection, namely: 1-, 3- and 7-monomethyl uric acids, 1,3-, 1,7- and 3,7-dimethyl uric acids and 1,3,7-trimethyl uric acid. The presence of a methyl group in position 7 appears to have an inhibiting influence on the development of the uric acid color reaction, the molecular value obtained in comparison to uric acid being: 1-monomethyl uric acid 85 per cent, 1,3-dimethyl uric acid 72 per cent, 3-monomethyl uric acid 29 per cent, 1,3,7-trimethyl uric acid 5 per cent and 7-, 1,7- and 3,7-methyl uric acids a mere trace of color.

It has been found that the methyl uric acids are all apparently quite stable in the animal organism, since the methyl uric acids which give the color reaction increase the color development for uric acid in the urine of the rat when given intraperitoneally and in the Dalmation dog when administered by mouth.

Although it is quite possible that the increased excretion of uric acid observed after the ingestion of caffeine and theophylline may result from a stimulation of metabolism, the facts noted above would be in harmony with the fact that theophylline and caffeine increase uric acid excretion while theobromine does not, as the latter could not cause an apparent increase in uric acid excretion as a result of oxidation in position 8 without previous demethylation, whereas theophylline and caffeine would give such an increase in color if oxidized in position 8 without or with incomplete demethylation.

NAKAHARA, WARO (TOKYO). Certain Nutritional Aspects of Tumor Growth: The Relation of Vitamin B.

The work of previous investigators indicated that tumor tissue can grow actively in animals kept on a vitamin B deficient diet inadequate to maintain the body weight. This did not settle the important question of whether or not vitamin B is essential for tumor growth. Our recent experiments showed that the growing tumor did not utilize the vitamin B in the body of the host. The experiments consisted of a comparison of the amount of vitamin B reserve in the liver of tumor bearing and non-tumor bearing animals, both kept under the dietary condition in which extraneous supply of vitamin B is excluded. Using the growth of young rats as the method of vitamin B assay, we found that the vitamin B stored in the liver is not depleted more rapidly in tumor bearing animals than in non-tumor bearing ones. In these experiments apparently the rapid growth of the tumors took place independently of the available vitamin B supply.

The possibility of the tumor tissue being capable of synthesizing vitamin B then came up for consideration. Many experiments, using both rats and pigeons, indicated that the Rous chicken sarcoma is habitually deficient in its vitamin B content, while Flexner-Jobling rat carcinoma and Fujinara rat sarcoma were found to contain this vitamin, but only in very small amounts. These facts may be taken to speak against vitamin B synthesis by tumor tissues, though they do not exclude that possibility entirely. However, a slight uncertainty regarding this point does not affect the conclusion that while normal tissue growth is absolutely dependent on extraneous vitamin B, this latter may be of no concern to the growth of malignant tumors.

That there seems to be a point of fundamental difference in the nutri-

tional requirements of normal and malignant tissue growths should justify a hope that there may exist some dietary factor essential for tumors and non-essential for normal tissues.

NAVEZ, A. E. and W. J. CROZIER (CAMBRIDGE, MASSACHUSETTS). **Carbon Dioxide Excretion During Geotropic Curvature of Roots.**

With standardized conditions of temperature, in darkness, and with a constant current of moist pure air, the rate of excretion of carbon dioxide by a growing root of *Vicia faba* remains constant over a very considerable period of time. When the seedling is geotropically excited by displacement through an angle of 90° , the rate of excretion of CO_2 increases, passes through a maximum at a time equal to about twice the measurable reaction time for the initiation of geotropic bending of the root, and then gradually declines until it assumes the same value as before excitation. Between the limits 7.5° and 22° , the areas under these curves are constant. At temperatures so low that no geotropic reaction definitely occurs, this rule is no longer obeyed. The rate of curvature at any moment definitely parallels that for rate of production of CO_2 . The termination of the process of curvature corresponds in time to the return of the curve of CO_2 excretion to the initial level. The temperature characteristic (μ) for the acceleration of CO_2 excretion ($16,200 \pm$) corresponds quantitatively with that for the resting level of production of CO_2 . These facts indicate that the acceleration of oxidative respiratory processes as a result of geotropic excitation is closely connected with the execution of the orientation.

NAVEZ, ALBERT E., B. B. RUBENSTEIN and W. J. CROZIER (CAMBRIDGE, MASSACHUSETTS). **Starch Hydrolysis as Affected by Polarized Light.**

The diastatic hydrolysis of soluble starch has been found to be accelerated to the same extent by either ordinary light or plain polarized light, provided they are of the same intensity and spectral composition, when the purification of the diastase has been performed in the absence of light. If the diastase be purified under usual laboratory illumination this effect is practically imperceptible.

The sensitization to light of the system starch plus diastase by the addition of dyes has been studied for several dyes of the fluoresceine group. At concentrations of 1:100,000 to 1:1,000,000 fluoresceine increases the rate of hydrolysis by about ten to twelve per cent, and the total amount of hydrolysis to about eighty-five per cent of the total possible hydrolytic splitting as compared to eighty per cent in tests without fluoresceine. Eosine Y and B, and erythrosine, at the same concentrations, produce about the same acceleration. These dye-stuffs exhibit different intensities of fluorescence, different fluorescence spectra, and different absorption spectra over a wide range. The acceleration therefore cannot be attributed to an optical activation by a fluorescence effect, but must be of photochemical type. When the solutions of dye-stuffs are used as external screens, no acceleration is obtained and the rate of hydrolysis is practically the same as with the dye-free solution. In all these experiments ordinary and plain polarized beams of the same intensity and the same spectral composition (up to 500 meter candles intensity, obtained by the use of very large Nicol prisms) have the same action.

NEEDHAM, J. (CAMBRIDGE, ENGLAND). **The Physiology of the Cleidoic Egg.**

It is pointed out that the eggs of some animals are more completely isolated from their environment than others, and the word "cleidoic" (from the Gr. κλειδω, shut off) is proposed as a designation of the "closed-box" condition. A typical non-cleidoic egg would be that of an echinoderm, which is not supplied by the maternal organism with sufficient ash or water to make one complete embryo, but has to absorb many of its constituents from the sea, while a typical cleidoic egg would be that of a bird, where all that the embryo requires, except the greater part of the oxygen, is provided within the closed system. Between these extremes, many intermediate grades are found.

The evolution of the cleidoic egg involved far-reaching metabolic changes in the succeeding ontogenies, for closure of the egg-system is accompanied by difficulties in getting rid of incombustible waste-products. Thus the eggs of birds, reptiles, and insects, combust markedly less protein during their embryonic life (in per cent of the protein initially present) than do the eggs of aquatic animals such as fishes and amphibia. Cleidoic eggs also produce as the main end-product of their nitrogenous catabolism, the comparatively insoluble and indiffusible uric acid, as opposed to non-cleidoic eggs in which the end-products are urea and ammonium salts. There is thus a clear correlation between terrestrial oviparous animals, and the power of forming uric acid from proteins (uricotelic metabolism). The combustion of fatty acids by cleidoic eggs is also relatively more intense than in non-cleidoic ones, probably no coincidence, in view of the metabolic water formed when fat is burned.

On these views, the mammalian embryo is an aquatic organism, its metabolism being adjusted to unlimited water intake and to the easy removal of waste, and the fact that mammals, although terrestrial animals, do not excrete their nitrogen in the form of rings, is thus explained. The cleidoic habit is connected also with other peculiarities, perhaps the most striking of which is the rapidity of avian incubation-time when compared with mammalian gestation-time, i.e., the fact that it takes considerably longer to make a mammal of given birth-weight than a bird.

NICE, L. B. (COLUMBUS, OHIO). **The Number of Erythrocytes in White Rats Under Different Experimental Conditions.**

Daily injections of one cubic centimeter of 1:25000 adrenalin chloride solution (Parke, Davis & Company) administered subcutaneously into both normal and adrenalectomized white rats caused an augmentation in the number of erythrocytes in the blood drawn from the heart, and this increase continued during the course of the experiment, fifty-six days.

Emotional excitement produced an increase in erythrocytes in the blood of normal rats but no change in the count of adrenalectomized or splenectomized rats.

This augmentation in erythrocytes seems to come from the reservoir in the spleen.

NISIMARU, YASUYOSI (OKAYAMA). **Study on the Bile Pigment Originating from Hemoglobin; No. 1.**

Ringer solution, kept at constant pressure and at constant content of oxygen was perfused through the liver (*Bufo japonicus*) from the hepatic

artery and the portal vein and came out from the hepatic vein. The bile clear as a water solution flowed from the cannula inserted into the bile duct. With this system the following experiment was performed. 1, O-Hb Ringer solution; 2, CO-Hb Ringer solution; 3, O-Hb added to 1/150 M HCN solution was perfused through the liver by the above mentioned method. The eliminated bile pigment was tested for the appearance of absorption bands in the visible portion and the ultraviolet portion of the spectrum and by the variation of color and the chemical reaction.

My conclusions were as follows:

1. When O-Hb Ringer solution was perfused through the liver the bile pigment was eliminated in the cannula of the bile duct.
2. The elimination of the bile pigment from the liver was influenced by poisoning with HCN, *i.e.*, it ceased entirely.
3. If CO-Hb Ringer solution was perfused through the liver, bile pigment was not eliminated.
4. When O-Hb Ringer solution was perfused through the liver from hepatic artery, the bile pigment was eliminated. While O-Hb Ringer solution was perfused through the liver from portal vein, bile pigment was not eliminated.

NITZESCU, I. I. et GR. BENETATO (CLUJ, ROMANIE). Action du pancréas endocrine sur la lipodierèse pulmonaire.

On a étudié l'action du poumon sur les graisses et sur le cholestérol par des recherches sur des chiens normaux et dépancréatés.

Des expériences "in vivo" (par des dosages des graisses et du cholestérol dans le sang du coeur droit et du coeur gauche) et "in vitro" (fragments de poumon en autolyse aseptique) sur des chiens normaux en pleine digestion des graisses, sur des chiens dépancréatés et sur des chiens dépancréatés et sous la pleine influence de l'insuline, on est arrivé aux conclusions suivantes:

Le poumon manifeste tant "in vivo" que "in vitro" une activité lipodierétique et cholestérololytique notable. L'exérèse complète du pancréas produit un trouble profond dans cette activité: la lipodierèse et la cholestérololyse pulmonaire "in vivo" est complètement disparue; la lipodierèse et la cholestérololyse "in vitro" subit une profonde diminution. L'addition d'insuline en poudre (Nitzescu) ou en solution (Lilly, Wellcome) à l'organe en autolyse aseptique ne confère aucun pouvoir lipodierétique ou cholestérololytique.

Au contraire, l'administration de l'insuline en injection sous-cutanée rétablit l'activité du poumon "in vivo" sur les graisses et sur le cholestérol au même niveau que chez l'animal normal. Aussitôt passée l'action de l'insuline, la lipodierèse pulmonaire disparaît de nouveau. De même "in vitro" le poumon manifeste une activité souvent plus accentuée que le poumon normal.

Il s'ensuit comme conclusion générale que l'action lipodierétique sert due à une diastase tissulaire—la *lipodierase*, qui ne pourrait actionner qu'en présence d'un coenzyme activateur—l'insuline.

NITZESCU, I. I., J. JACBOVICI et A. POP (CLUJ, ROMANIE). Sur le rôle de la glande carotidienne chez l'homme. Recherches expérimentales.

L'excitation faradique directe de la glande carotidienne chez l'homme,

déclenche un réflexe cardio-vasculaire qui s'est traduit toujours dans nos recherches par un réflexe dépresseur analogue au réflexe sino-carotidien décrit par Hering.

L'excitation mécanique de la glande par compression digitale ou par la pince anatomique peut aussi produire un réflexe dépresseur moins accusé.

L'excitation faradique directe du sinus carotidien, surtout après l'exérèse de la glande, ne produit aucun effet cardio-vasculaire.

L'excitation mécanique du sinus par compression digitale après l'extirpation de la glande produit des effets insignifiants.

Les réflexes sino-carotidiens et surtout le réflexe dépresseur sino-carotidien de Hering semble se produire—au moins chez l'homme—par l'intermédiaire de la glandule carotidienne qui serait un organe récepteur des excitations ayant leur point de départ au niveau de la bifurcation de la carotide. Ce réflexe serait, par conséquent, plutôt un réflexe glandulo-sino-carotidien que sino-carotidien et il aurait un rôle dans le maintien de la pression sanguine au niveau normal.

L'exérèse de la glande carotidienne est suivie en général d'une augmentation plus ou moins accusée, mais constante, de la tension artérielle.

Toutes ces considérations suggèrent la possibilité d'appliquer un traitement chirurgical, par exérèse de la glandule intercarotidienne, dans quelques états d'hypotension vasculaire permanente.

NOLF, P. (BRUXELLES). Influence de l'anoxémie sur le plexus nerveux entérique.

Une anse intestinale de coq domestique longue de 12 à 15 cm. suspendue en liquide de Ringer oxygéné et supportant une pression intérieure de 15 cm. d'eau exécute des contractions péristaltiques vigoureuses, qui sont l'expression motrice d'influx nerveux parcourant d'avant en arrière la chaîne ganglionnaire du système nerveux entérique. Celle-ci est formée d'une succession de neurones, appelés connecteurs, placés à la file et dont les synapses sont disposés de telle façon que l'influx nerveux ne puisse circuler que dans le sens oral-aboral. Des neurones connecteurs, l'influx nerveux se propage aux fibres musculaires par l'intermédiaire d'une assise de neurones interposés, les neurones moteurs.

La stimulation faradique de l'extrémité orale y fait naître des ondes péristaltiques semblables aux ondes spontanées, s'étendant comme elles jusqu'à l'extrémité aborale. Si l'on substitue un courant d'azote au courant d'oxygène qui traverse le liquide de Ringer, les contractions péristaltiques spontanées s'atténuent progressivement. Elles sont remplacées après quelque temps par des contractions de segmentation. Ultérieurement l'anse devient complètement inerte.

Peu après la substitution de l'azote à l'oxygène, la stimulation faradique de l'extrémité orale provoque une contraction étendue à toute l'anse qui se distingue de la contraction en milieu oxygéné par plus de précocité et plus d'intensité. Ultérieurement l'aire de la réaction motrice se rétrécit progressivement à une distance de plus en plus courte de électrodes. Enfin toute réaction au courant faradique disparaît. L'anse est encore capable de se contracter sous l'influence de l'acétylcholine, de la pilocarpine, du chlorure de baryum.

L'anoxémie poussée à ce point paralyse les cellules du plexus entérique et les fibres de Remak.

Le retour à l'oxygène rend à ces éléments leurs propriétés physiologiques. L'immersion d'un nerf mésentérique dans du Ringer privé d'oxygène par un passage prolongé d'azote supprime la conduction après moins de dix minutes dans les fibres post-ganglionnaires du nerf (fibres de Remak). La substitution de l'oxygène à l'azote est suivi de la restauration de la fonction nerveuse après dix minutes.

DU NOÛY, P. LECOMTE (PARIS). **On the Nature of the Changes Occurring in the Properties of Serum Heated at 56°-57°.**

We have shown (Journ. Gen. Physiol., 1929) that, in addition to deep biological changes, blood serum heated progressively from, say, 20°C. up to 70°C. manifests an absolute minimum of viscosity at a temperature near 56°. It appeared to us that there might exist a common underlying cause of chemical nature. In order to elucidate this point, serum was heated at different temperatures in sealed tubes, and its rotatory power determined. It was thus found: 1, that for short heating, there was no coefficient of temperature between 0° and 50° (showing that no structural changes occurred in the molecule) and 2, that the negative rotatory power increased after 55° was reached. At 57°-58°, the rate of increase became greater, and around 60° it became very important, even for five minutes' heating. The curve expressing the values of α , plotted against temperature, runs parallel to that expressing the viscosity under the same conditions. It thus seems that the existence of the common underlying chemical phenomenon is proven. Its nature is being investigated.

VON OETTINGEN, W. F. (CLEVELAND). **Simultaneous Cinematography of Intestinal Movements and Tracings.**

In this film a short piece of rabbit small intestine is perfused by the Bauer method, the activity of the longitudinal muscles is recorded by direct transmission to a muscle lever, the activity of the circular muscles is registered by the changes of the internal pressure as reproduced by a tambour, the output is recorded by the discharge of an Archimedes bucket, each discharge being marked by an electric signal on the drum and the time is given in minutes. By means of a mirror arrangement the tracing and the contracting intestine are photographed simultaneously.

OLMSTED, J. M. D., H. MACKLER and W. W. SIMPSON (BERKELEY). **Relation of Phosphocreatine to Lactic Acid in Frog Muscle.**

One-third of a quickly excised gastrocnemius (weight of whole muscle, 12 grams) was sliced off, frozen in liquid air and estimations made of phosphocreatine and lactic acid. The remainder of the muscle was stimulated with break shocks at 3 second intervals for 5 minutes; one-half of it was then frozen. The remaining third was stimulated for another 5 minutes, then frozen.

The phosphocreatine decreased in the successive thirds of such a worked muscle, and the lactic acid increased, but not proportionately. Much more lactic acid appeared than could be neutralized by the amount of phosphocreatine hydrolyzed.

As a control, the opposite gastrocnemius was removed, and treated in the same way except that it was allowed to stand without stimulation. In this case the phosphocreatine remained practically constant in the successive slices of muscle, but there was a gradual increase in lactic acid, the

third portion having often twice as much lactic acid as the first, but without hydrolysis of phosphocreatine taking place for neutralization.

These results seem to indicate that hydrolysis of phosphocreatine occurs during muscular contraction in quantities quite insufficient to buffer the lactic acid produced, whereas in cut muscle allowed to stand lactic acid is formed without accompanying hydrolysis of phosphocreatine.

ORBELI, Z. A. (LENINGRAD). **Effect of Sympathetic on Muscle and Central Nervous System.**

ORTH, O. S., M. E. McENDORFER, F. C. GREEN and W. E. BURGE (URBANA, ILLINOIS). **Proof that an Abrupt Rise in Temperature Greatly Increases the Catalase Content of Pine Needles.**

In February, 1929, when the temperature was -10°C . and had been continuously below zero for several days, two branches were cut from the same limb of a large pine tree (*Pinus strobus*) and brought to the greenhouse. Catalase determinations of the needles of both branches were made immediately. This was done by removing some of the needles from the branches and grinding them twice through a small hashing machine. One gram of this ground material was added to 25 cc. of neutral hydrogen peroxide at 22°C . in a bottle to which one gram of calcium carbonate had been added and the amount of oxygen liberated in fifteen minutes was determined. Each branch was then stood in a pail of water and one was placed outside the greenhouse, where the average temperature for the succeeding eight days was -5°C ., and the other was kept inside where the temperature for the first four days was 22°C . and the succeeding four days it was 30°C . Catalase determinations were made daily during the eight day period of the needles of the branch kept in the greenhouse as well as of the needles of the branch kept outside in the cold.

The amount of oxygen liberated by the needles of both branches when they were brought to the laboratory was 6 cc. and 7 cc. respectively. The needles of the branch kept outside at the low temperature continued to liberate approximately the same amount of oxygen daily throughout the eight day period of the experiment, while the needles of the branch kept inside at the higher temperature rose and the last day of the experiment these needles liberated 75 cc. of oxygen. Hence the effect of a rise in temperature was to cause an increase from 6 cc. to 75 cc. in oxygen liberated by the needles. From this it is concluded that a rise in temperature greatly increases the catalase content of pine needles.

OSTERHOUT, W. J. V. (NEW YORK). **Bioelectrical Phenomena.**

When a cell of *Nitella* is cut a wave passes rapidly along the cell: at each spot it touches a characteristic death process is brought about. In dilute solutions (e.g., 0.001 M KCl) there is a sudden change making the protoplasm more negative: in the more concentrated solutions (e.g., 0.1 M KCl) the protoplasm becomes more positive. Hence the current of injury may be made positive or negative.

The death curves thus obtained may be explained (and in fact predicted) by assuming that the protoplasmic layers (which have been demonstrated by bioelectrical tests) are oppositely charged and that the outer protoplasmic layer is more rapidly altered with 0.1 M KCl and the inner with 0.001 M KCl.

In addition to this waves of negativity, resembling in form and magnitude those of muscle and nerve, occur spontaneously and are often rhythmic in character. They may be induced in a variety of ways (touching, bending, application of solutions, etc.). The fact that a wave cannot pass a spot made negative by the application of 0.1 M KCl suggests that in order to be stimulated the protoplasm must be positively charged. This and other facts are discussed from a theoretical standpoint.

The *Nitella* cell acts in many respects like a single fibre of muscle or nerve and this has led to experiments on muscle and nerve which lead to some interesting viewpoints (e.g., that the surface of the muscle is dual in character).

PACK, GEORGE T. and DONN BARBER (NEW YORK). **The Placental Transmission of Insulin from Fetus to Mother.**

Insulin is transmitted through the placenta of the goat from fetus to mother, as determined by variations in maternal blood-sugar levels following intrafetal injection of commercial insulin. The experiments were carefully controlled by the previous determinations of glucose tolerance under the same conditions.

PALLADIN, ALEXANDER (KHARKOV). **Investigations of the Biochemistry of Creatine Phosphoric Acid and Other Phosphorus Compounds of the Muscles.**

Creatine phosphoric acid is one of the substances producing energy in the muscles. The determination of the rôle it plays in the muscle will doubtless lead to the discovery of the rôle of creatine; as yet the connection between the transformation of creatine and muscular action has been unknown, except for the fact, discovered by A. Palladin and Ferdmann, that muscles under training are enriched with creatine. The investigations made in the Ukrainian Biochemical Institute in *Kharkov* were undertaken with a view of studying the biochemistry of the creatine phosphoric acid and its transformation in the muscles, as well as that of other phosphoric acid compounds, and they were also done in order to find the relationship existing between these substances and the creatine phosphoric acid.

After the properties of creatine phosphoric acid and the method of its determination were studied, it was found that muscles having different functions contain various amounts of phosphocreatine and that white muscles, capable of swift contractions, always have more of it; smooth muscles also have phosphocreatine like a number of other organs. A study was made of the influence of several factors altering the creatine content of the muscle exercise on the phosphocreatine of the same.

Investigations performed with the training of muscles have shown that under training the content of creatine phosphoric acid rises; hexose monophosphoric acids are far from increasing and they even diminish slightly; the content of the muscles in pyrophosphoric acid remains unchanged.

During strong muscular contractions (cramps produced by means of strychnine), the phosphocreatine of the muscles falls markedly, but their reserves of that substance are not wholly exhausted; pyrophosphate also shows a decrease.

Creatine phosphoric acid is also contained in the brain (in the hemispheres as well as in the cerebellum); mammals having more thereof than birds.

During short autolysis (10-30 min.) the muscles of pigeons show a decrease of ortho- and pyrophosphoric acids; meanwhile orthophosphoric acid serves to build up hexose phosphoric acid, so that the amounts of the same increase proportionately.

Hexose phosphoric acid (real lactacidogen) is found in white and in red striped muscles: in the former there is a greater amount of that acid, while the latter have it in smaller amounts. Contrary to the old view it is also found in smooth muscles and in the brain, the latter holding a place between the striped and the smooth muscles with regard to its phospho-creatine content.

Under the influence of insulin the lactacidogen of rabbits' muscles increases.

PARNAS, J. K. (Lwów). Ammonia Formation in Muscle and Its Source.

In further investigation of the ammonia formation, which was found, by Parnas and Mozokowski, to occur with traumatic injury, survival, and every kind of rigor of muscle, special attention was given to the question of ammonia formation during activity and to its sources. Muscular activity is always, without exception, associated with ammonia production: the rate of ammonia formation is closely proportional to the product *tension* \times *length* developed, independent of oxygen supply, and irreversible; there is in isolated frog muscle no reaction, converting ammonia once split off into its precursor or into any other compound. The rate of ammonia formation for unity of *tension* \times *length* varies with the season, and falls from 0.01 mgm. NH₃ nitrogen for 100 kgm. \times cm. in summer to about 0.002 mgm. which is found in starving frogs during January. In the following months it rises again.

The source of traumatic ammonia formation, as well as of the ammonia produced during anaerobic activity, is the adenine nucleotide; its conversion into inosinic acid was proved by direct experiments, in which free and combined purine bases have been determined. But when frog muscles are working without fatigue, in oxygen, no decrease of the adenine content can be observed, while there is a large ammonia formation. Adenine nucleotide is restored, under these conditions, from inosinic acid, not by utilisation of ammonia once split off, but probably by oxidative deamination of amino acids or their derivatives. In this way the adenine nucleotide acts like a body, which is able to give off ammonia rapidly, independently of oxygen and oxidations, and which is restored in the slow recovery processes, which occur only in the presence of oxygen. In living muscle the system adenine nucleotide \rightarrow inosinic acid does oscillate between its two components, ammonia being discharged during activity, recharged during recovery. It seems not improbable, that the aminopurines in nucleic acids should have the same function.

PATTERSON, T. L. (DETROIT). Gastro-Tonic Automatism as the Determining Factor in the Type of Muscular Response of the Stomach of the Monkey.

Previous studies on the movements of the empty stomach of Javanese monkeys recorded by the balloon method after an 18 to 24 hour fast, have

demonstrated that the contractions are practically identical with those of the human stomach. Earlier phases of this work indicated considerable fluctuations in gastric tone. As a result a series of acute experiments was inaugurated on Javanese and Ringtail monkeys (*Macacus irus* and *Macacus rhesus*) in an attempt to determine the effects of nerve influence on the tonus and motor activity of the gastric mechanism. Twenty-nine animals were used including one baboon (*Cynocephalus anubis*). The experiments were performed under light ether anesthesia in order to preserve the reflexes. The vagi, carotids and esophagus were exposed in the neck. A lateral incision in the esophagus admitted the stomach balloon connected with a water manometer for recording the gastric movements. The blood pressure from the carotid or femoral artery was recorded simultaneously.

Stimulation of the central end of the vagus or sciatic results in either an augmentatory or an inhibition of the stomach, the reaction appearing to be primarily dependent upon the pre-existing state of tonus of the gastric musculature itself. If the stomach is hypertonic, reflex inhibition will follow central stimulation of these nerves; if hypotonic, a contraction may occur or there may be a definite increase in the tonus. Stimulation of the peripheral end of either vagus produces a somewhat similar inhibitory or augmentatory action depending upon the degree of gastric tone. Peripheral splanchnic stimulation may also exert a similar but smaller response, while central stimulation with opposite splanchnic intact produces at least a reflex inhibition of tone. The gastric response is, therefore, dependent upon the existing tonic state of the peripheral mechanism which may involve both tonus and movement, these varying quite independently of each other.

PAVLOV, I. P. (LENINGRAD). Inhibition in the Normal Activity of the Cerebral Hemispheres.

When studying the normal activity of the cerebral hemispheres by the method of conditioned reflexes, one notices the continual participation of the process of inhibition. Two rôles of the inhibitory process may be distinguished. The first rôle is the protection of the cortical cells from excessive functional destruction caused by strong stimuli; the second rôle, the protection of these same cells from useless work. Every time, when a very strong external stimulus is applied, or the whole irritability of the cortex is very markedly raised (caffein), or at least (in our experiments with the conditioned alimentary stimuli) when the alimentary excitability is intentionally raised by producing a certain degree of hunger or by giving a special sort of food, in all these cases the inhibition is interfered with. On the other hand, as soon as the conditioned stimulus as a signal, is not accompanied by the unconditioned stimulus, or this does not come at the proper time, for instance too early, inhibition rapidly appears. In all the above mentioned cases, the action of the inhibition is markedly increased when bromide is introduced. Thus bromides should be considered as an agent especially connected with the inhibitory process. This agent increases inhibition and it may be regarded as an indicator of the presence of inhibition in a given nervous process. The next problem which is to be solved may be formulated in the following question: is it possible to accept a single basis to both of the rôles of inhibition described above?

PEREIRA, JAYME R. (S. PAULO, BRAZIL). **On the Action of Arnica upon the Blood Pressure and Respiration in Dogs.**

Injection of *arnica* fluid extract into the femoral vein of a dog causes a fall of blood pressure accompanied sometimes by the disappearance of the respiratory movements, this depending upon the dose used and the actual condition of the animal.

During the phase of apnea, which is sometimes short, but which may be very long (up to 8 minutes), the heart maintains its beating level, begins to rise again very gradually and may attain a level much higher than that which occurred before the drug's action. After attaining the maximal height, it falls again very slowly until the heart stops. The amplitude of the heart beats during the blood pressure's gradual elevation also increases gradually, and diminishes gradually until its complete disappearance.

The respiration in some cases reappears and may regain its normal rhythm, but in the majority of cases it stops definitely, while the heart continues beating.

Apnea of 5 minutes' duration with spontaneous recovery of the respiration was observed in some instances. The first respiratory movements were followed immediately by extraordinary elevations of the blood pressure.

Studies are being continued in order to investigate a possible part played by the adrenal glands in the production of the rise in blood pressure during the apnea phase and that which follows the first spontaneous respiratory movements after this phase.

As the plant fluid extract is made up with alcohol, control experiments were done in which it was observed that the alcoholic fraction of the drug has no influence on the observed phenomena here described.

PERLZWEIG, WILLIAM A. (BALTIMORE). **The Organic Acids of the Blood and Urine.**

An attempt was made to determine quantitatively the organic acids in normal and pathologic samples of blood and urine by means of the electro-metric titration method previously described (W. A. Perlzweig and G. Delrue, Proc. Soc. Exp. Biol. and Med., 1928, xxv, 548). The quantities and concentrations as well as the chemical nature of the acids found varied with the methods employed for the removal of protein, phosphates, bases and of the other interfering substances from the blood or urine. Thus in blood the highest concentrations were found after the removal of protein by HPO, followed by lime (7-15 milliequivalents per liter). Somewhat lower figures (4-8 milliequivalents) were obtained after the use of Hg salts or of phosphotungstic acid. Still lower figures (3-5 milliequivalents) resulted from the use of picric acid. Extraction of the acids with lipid solvents (ether, toluol, benzene, etc.) yielded the lowest amounts (1-3 milliequivalents). The same approximate sequence of results was obtained with normal urines. These results taken in conjunction with the nature of the titration curves lead to the following suggestions:

1. The lower fatty acids extractable with ordinary organic solvents are present in normal blood and urine in very low concentrations.

2. The ordinary methods for the titration of organic acids, such as Palmer and Van Slyke's method, yield results which undoubtedly include a variety of organic bases and protein cleavage products (polypeptides, oxy-proteic acids) which may be removed by picric acid, phosphotungstic acid, salts of heavy metals. These substances appear to constitute the greater part of the so-called "organic acids" of the physiological fluids, titratable between pH 2.5 and 8.5.

Increased concentrations of organic acids in the blood and urine were observed in cases of pneumonia, uremia of acute nephritis, and in nephrosis.

PETERSON, VERNON L. and EDWARD S. WEST (ST. LOUIS). **Reducing Fermentable and Non-Fermentable Substances in Normal and Pathological Urine.**

The reducing fermentable and non-fermentable substances in normal and pathological urines have been re-investigated by an improved technique. Urine filtrates prepared by mercuric sulphate precipitation as recently described for blood¹ were fermented by yeast according to Somogyi. Reducing substances were determined in the filtrates before and after fermentation using an improved iodometric copper reagent. In fifty normal urines the daily excretion of fermentable substances varied widely up to a few hundred milligrams. The excretion of reducing non-fermentable substances was more constant averaging about 0.4 gram per day (in terms of glucose). It seems to bear no simple relation to body weight, diet, exercise or volume of urine but to be somewhat characteristic of the individual. Patients with renal disorders excreted less or even none of the non-fermentable substances. The amount of such substances excreted may prove of value as an index of renal function. Mercuric sulphate filtrates of urine contain 12-25 mgm. of nitrogen per 100 cc. of urine and it is possible that some of the reducing non-fermentable substances may contain nitrogen, contrary to present opinion. The fermented mercury filtrates do not absorb iodine in acid but do so in slightly alkaline solution, which suggests the presence of aldose. A crystalline phenylhydrazine derivative, presumably an osazone, has been isolated from such filtrates in quantities which seem to indicate that a considerable fraction of the reducing non-fermentable substances is sugars, as suggested also by the work of Baisch, Lemaire, Patterson and others.²

PICKFORD, MARY³ and E. B. VERNEY (LONDON). **The Response of the Isolated Kidney to Ligation of a Primary Arterial Branch.**

When the two kidneys of a dog are perfused in parallel by means of a heart-lung preparation, the rate of flow and the composition of the urine from the one are approximately equal to those of the urine from the other. Moreover, the response of the one to a given change in the conditions of perfusion approximates closely to that of the other. With such a preparation we are investigating the effects on the secretion of urine of ligation of a primary branch of the renal artery.

¹ West, Scharles and Peterson. *Journ. Biol. Chem.*, 1929, lxxxii, 137.

² Baisch. *Zeitschr. Physiol. Chem.*, 1895, xx, 249. Lemaire. *Ibid.*, 1895, xxi, 442. Patterson. *Biochem. Journ.*, 1926, xx, 651.

³ Working with a grant from the Medical Research Council.

In all experiments so far performed the resultant diminution in urine flow expressed as a percentage of the control rate of flow has been less than the diminution in blood flow similarly expressed. Indeed, not infrequently an absolute increase in urine flow occurs at constant perfusion pressure. The increase is immediate in its onset, and is accompanied by a change in composition of the urine, a change, moreover, which characterizes it as a "pressure" diuresis.

In some experiments a dye has been added to the blood shortly before the close of the experiment, and the ratio between the perfused and infarcted portions of the renal cortex determined later by weighing. There is close agreement between the figures giving the percentile reduction in blood flow through the kidney and those giving the percentile reduction in renal cortex. The rate of blood flow through the still functioning part of the kidney is therefore not appreciably changed by ligaturing the arterial supply to the remaining part.

The mechanism by which one part of the isolated kidney becomes cognizant of the arrest of the blood supply to the remainder, and responds to this arrest by secreting more urine—a strictly local mechanism, since no polyuric response is given by the control kidney—is being more fully investigated.

PIERACH, ALEXANDER (MÜNCHEN). **Über die Analyse des Perkussions-schalls, der Atemgeräusche und Herztöne.**

Vermittels eines Kondensatormikrophons, einer Verstärkerapparatur und eines Oscillographen werden Perkussionsschall, Atemgeräusche und Herztöne frequenz- und amplitudengetreu registriert.

Das Klangbild der vergleichenden Perkussion (Finger-Finger-Perkussion) bei einem einseitigen pleuritischen Exsudat ergibt:

a. für den normalen Lungenschall: im Beginn eine rasche Welle von 250 H und dann mehrere fast rein sinusförmige, gedämpfte Schwingungen von 72 H. Diese sind für den Lungenschall charakteristisch.

b. für das Exsudat: eine einzige, fast sinusförmige Schwingung von 235 H.¹ Dasselbe Klangbild wie auf der Seite des Exsudats erhält man auch, wenn man Finger-Finger in freier Luft perkutiert. Es muss also diese Schwingung im Anfang einer jeden Finger-Finger-Perkussionskurve enthalten sein. So ist auch die erste Schwingung im Klangbild des Lungenschalls als Aufschlag der beiden perkutierenden Finger zu erklären.

Es werden Versuche über den Anschlag freischwebender und stark gedämpfter Systeme an Stimmgabeln und Resonatorkästen gemacht. Das Klangbild des Anschlags wird registriert und zeigt grosse Verschiedenheiten je nach der Art des Anschlags bzw. der Perkussion. Aus diesen Versuchen ergibt sich, dass die Finger-Finger-Perkussion der Hammer-Plessimeter-Methode in den meisten Fällen überlegen ist. Denn die Finger-Finger-Perkussion gibt am besten und reinsten den normalen Lungenschall wieder. Der Vergleich der Klangbilder dieser beiden Methoden zeigt das eindrucksvoll.

Der Bauchschall zeigt fast rein sinusförmige, gedämpfte Schwingungen um 200–300 H.

¹ Wie Kucharski (Compt. rend. des Séances de la Société de Biologie, xc, 1924) gezeigt hat, genügt eine einzelne Schwingung dazu, um dem Ohr die Tonhöhe zu charakterisieren.

Das normale Atemgeräusch der Lunge (Vesikuläratmen, Inspirium) setzt sich zusammen aus einer Hauptschwingung um 100 H. und Oberschwingungen um 500 H. (s. auch Brandi und Fahr, Arch. f. klin. Med. 164). Durch die Analyse einer solchen Kurve mit dem Maderschen Analysator konnten Oberschwingungen von 870 H nachgewiesen werden. Die Amplitude der Grund- und Oberschwingungen und ihre prozentuale Verteilung im Klangbild des Atemgeräusches wechselt von Fall zu Fall erheblich und erklärt so die Verschiedenheit des normalen Vesikuläratmens.

Im In- und Expirium sind aber auch noch tiefere Frequenzen um 50-60 H enthalten. Diese entsprechen dem Muskelton der Atmungsmuskulatur und sind nicht zum eigentlichen Atemgeräusch zu rechnen. (Dies konnte durch vergleichende Aufnahmen an einem Fall einer einseitigen Pleuritis exsud. nachgewiesen werden.)

Das Klangbild des Trachealatmens zeigt vorwiegend Frequenzen um 500 H. Fr. v. Müller konnte zeigen, dass im Trachealatmen aber auch die tiefen Teiltöne des Vesikuläratmens enthalten sind. Die Madersche Analyse eines solchen Klangbilds ergab eine Grundschiwingung von 130 H.

Die Aufnahmen der Herztöne ergeben:

a. für den ersten Herzton mehrere, fast sinusförmige Schwingungen um 30 H.

b. für den zweiten Herzton im Anfang eine einzelne Schwingung von 50 H und dann mehrere gedämpfte Schwingungen kleiner Amplitude unter 30 H. Der Abstand zwischen erstem und zweitem Herzton beträgt 0,29 Sek. Die pathologischen Herzgeräusche liegen in höheren Frequenzgebieten und sollen weiter bei gleichzeitiger Registrierung mit dem Elektrokardiogramm studiert werden.

Durch die Anwendung elektrischer Tonfilter sollen die bisherigen Ergebnisse überprüft und das Gebiet weiter durchforscht werden.

PIÉRON, H. (PARIS). Une méthode pour l'étude des lois d'établissement du Chroma d'une sensation lumineuse colorée.

Un spectrophotocolorimètre a été construit (par les soins des constructeurs Jobin et Yvon), qui permet de comparer à une plage éclairée par une lumière monochromatique de λ réglable (et dont on peut faire varier à volonté l'intensité et la pureté) une autre plage, éclairée dans les mêmes conditions, de façon indépendante, mais où la lumière monochromatique (de λ , d'intensité et de pureté réglées) se substitue, pendant un temps réglable à volonté, à une lumière blanche d'intensité égale.

On peut, dans ces conditions, en réglant la première plage pour qu'elle paraisse identique à la seconde, suivre l'évolution dans le temps du "chroma," au cours d'une impression lumineuse d'intensité invariable. Les premières recherches effectuées par cette méthode ont permis de vérifier certaines déductions dégagées de la théorie des couleurs subjectives de Fechner-Benham (*Année Psychologique* xxiii; 1923): le "chroma" comme la luminosité croît en fonction du temps et dépasse passagèrement le niveau d'équilibre (ondulation de Broca et Sulzer); les constantes d'établissement du chroma varient avec les couleurs, l'établissement étant nettement plus rapide, en particulier pour le rouge que pour le bleu; enfin la vitesse d'établissement est fonction de la pureté (depuis le seuil de perception du chroma jusqu'au chroma maximum).

Voici, d'après des expériences préliminaires, quelques valeurs numériques

obtenues: pour une lumière rouge (640 $m\mu$), l'intensité 1 étant l'intensité maxima que donne l'appareil:

	INTENSITÉ:							
	1	1	0,5	0,5	0,5	0,5	0,1	0,1
Pureté.....	0,2	0,5	0,1	0,2	0,5	1	0,2	0,5
Durée liminaire (en σ)	13	(moins de 5)	45	27	15	(moins de 5)	46	16

Même lumière, saturation perçue en fonction de la durée, ($I = 0,1$, $p = 0,5$), évaluée en pureté de la plage égalisée.

Temps d'action.....	106 σ	172 σ	224 σ	∞
Saturation.....	0,39	0,63	0,80	0,50

En lumière bleue (475 $m\mu$), la saturation maxima ($I = 1$, $p = 1$) est obtenue au bout de 218 σ , au lieu de 115 σ avec le rouge (640 $m\mu$ $I = 1$, $p = 1$).

Cette méthode permet seule d'étudier les lois du temps pour le chroma indépendamment de l'intervention des lois propres d'établissement du processus lumineux.

PI-SUÑER, A. (BARCELONA). Pulmonary Sensibility.

Through investigations which were already begun in 1918 we suggested the existence of a pulmonary sensibility that answers to differences of composition of the alveolar air. Our experiments on circulation in the head of a dog B with the blood furnished by a dog A through carotido-jugular anastomosis (1919) proved that variations in the concentration of CO_2 in the air, produce reflex effects on the movements of respiration.

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J. F. and C. Heymans perfecting this method (dog with two heads) performed the decapitation leaving between the head and the trunk of the dog B only the pneumogastrics. They confirmed the respiratory reflexes of chemical origin. The proportion of CO_2 in the blood that circulates through the heart and the aorta influences the respiratory regulation by a reflex mechanism. There is a cardio-aortic zone sensible to the humoral changes and the properties of its surroundings.

But this fact is not incompatible with the existence of pulmonary sensibility. Heymans supposed that lungs do not feel the changes in the composition of the blood which feeds them. Our last experiments prove that respiratory reflex responses may be attained according to the concentration of CO_2 in the air breathed, in spite of the exclusion of every circulatory agent.

We worked with the isolated head after the method of Heymans, with direct vascular anastomosis. We allowed the trunk B to die through haemorrhage. Once the heart has stopped beating one can still observe that an addition of CO_2 (to 25 per cent) to the air furnished to the trunk

B (by a blower for artificial respiration with constant rhythm and pressure, is the cause of modifications in the respiratory movements of the head which become more frequent or more profound. The double section of the pneumogastrics, of course, causes these effects to disappear. It elicits also some respiratory changes suggestive of the existence in the intact animal of a vagal tonus independent of mechanical respiratory factors.

PI SUÑER, SANTIAGO (ZARAGOZA). Formation de l'ammoniaque et rôle du rein.

Nos idées sur le lieu de formation de l'ammoniaque urinaire ont changé beaucoup dans ces dernières années. Après toute une série de travaux de plusieurs auteurs sur cette question, on commence à croire aujourd'hui que le lieu réel de formation de l'ammoniaque est le rein et que d'autre part cette fonction est un processus local de défense du rein pour empêcher la sécrétion d'une urine trop acide, processus local qui cependant est un des éléments constitutifs du mécanisme général de régulation de l'équilibre acide-base.

Dans une série de travaux sur le chien, nous supprimons, par section des filets nerveux et pinceautage du hile à l'acide chlorhydrique, tout contrôle nerveux dans un des reins, tandis que l'autre reste intact. Nous produisons alors un état d'acidose par injection intraveineuse d'acide chlorhydrique, et étudions les modifications du pH et de la teneur en ammoniaque de l'urine recueillie de chaque côté par cathétérisme urétéral. Tandis que le rein normal répond tout de suite à l'acidose par une élévation considérable du taux de l'ammoniaque, qui peut atteindre dix fois sa valeur primitive, et, après un certain temps, par un léger abaissement du pH, le rein de l'autre côté qui est énérvé reste tout à fait insensible à l'acidose. Son urine ne se modifie pas: le taux de l'ammoniaque reste le même, ainsi que le pH.

Dans la même série de travaux nous avons pu faire une autre observation. La réponse maxima du rein sain à l'acidose, réponse qui se manifeste surtout, comme je l'ai dit, par une élévation considérable du taux de l'ammoniaque, est suivie après quelque temps d'une oligurie presque complète. En opposition avec le rein énérvé, qui au contraire sécrète encore une quantité plus grande d'urine, le rein sain ne sécrète déjà plus. Nous interprétons ce phénomène comme l'expression d'un mécanisme défensif: le rein a déjà épuisé sa capacité locale de neutralisation des acides en excès du sang par formation d'ammoniaque; il faudrait éliminer une urine trop acide et par suite irritante. Alors le rein ne sécrète plus.

Nous pouvons résumer ainsi nos travaux:

1. Le rein est le lieu de formation de l'ammoniaque urinaire.
2. Pour que cette fonction se réalise dans le cadre des processus physiologiques, l'innervation normale du rein doit être intacte.
3. L'oligurie qui dans ces conditions fait suite à la réponse active du rein intact est l'expression de son épuisement fonctionnel.

PI-SUNYER, J. (BARCELONA). Blood in Cyanhydric Intoxication.

The research of A. Pi-Suñer (1927-1928) proved that cyanhydric intoxication is, at the same time, the cause of both hyperlipemia and hyperglycaemia. The author attributes it to a reaction of the organism due to difficulties regarding cellular oxidation.

Our investigations had the purpose of proving that the reducing activity of yeast and tissues of animals poisoned with cyanides is remarkably modified.

POLTYREV, S. S. und G. P. ZELIONY (LENINGRAD). **Der Hund ohne Grosshirn.**

Der Hauptzweck dieser Arbeit war den minimalen Teil des Grosshirns zu bestimmen, der dazu nötig ist, die bedingten (assoziativen) Reflexe auszubilden. Dafür wurden beim Hunde die beiden Grosshirnhemisphären entfernt, dabei blieben jedoch nicht nur beide Corpora striata, sondern auch eine dünne Schicht von Gehirngewebe in ihrer Umgebend erhalten; diese Schicht war rechts dicker, als links. Ausserdem wurde links ein kleiner Teil des Temporallappens an der Gehirnbasis zurückgelassen. Rechts ist der Rest des Temporallappens ganz gering. Die rechte Hemisphäre wurde am 28/X-1927 und die linke 30/XI-1928 entfernt.

Der Hund gleicht in seinem allgemeinem Verhalten einem Hunde mit völliger Exstirpation der Gehirnrinde. Diesem Hunde fehlt jede Orientierung, er reagiert nicht auf das ihn Umgebende und stösst sich fortwährend an verschiedenen Gegenständen. Oft fängt er an, nachdem er sich in einen Winkel verschlüpft hat, mit der Pfote an die Wand zu schlagen und auf dieselbe zu klettern. Er stellt sich dann auf seine Hinterpfoten und schlägt während langer Zeit mit seinen Vorderpfoten an die Wand, wobei er manchmal mit dem Schwanz wedelt. Oft beobachtet man bei diesem Hunde, wie auch bei anderen Hunden ohne Grosshirn, spontane Kaubewegungen, die von einer Speichelabsonderung gefolgt werden.

Bei Reizung der Pfote mit starkem faradischen Strom macht der Hund nie den Versuch sich zu flüchten (während des Versuchs wird der Hund im Gestell nicht immobilisiert). Er winselt dann stark, bellt kläglich und hebt die Pfote manchmal so hoch, dass er oft sein Gleichgewicht verliert und umfällt. Manchmal legt er sich auf den Rücken und erinnert an normale Hunde, wenn man sie prügelt oder wenn sie von anderen Hunden überfallen werden.

Die bedingten Reflexe, die von Gesichts-, Geruchs- und taktilen Reizen abhängen und an das Fressen gebunden sind, fehlen,—der Hund reagiert nicht auf das Futter, welches vor seiner Schnauze liegt und letztere sogar berührt. Die Nahrung (Fleisch), die in die vordere Hälfte der Mundhöhle gelegt wird, fällt heraus, und nur das in die hintere Hälfte der Mundhöhle gelegte Fleisch ruft ein Kauen und Schlucken desselben hervor. Das von einer Chininlösung benetzte Fleisch wird vom Hunde verschluckt, und nur wenn das Fleisch mit Chininpulver bestreut ist, wirft der Hund das Fleisch aus dem Maule heraus. Die Absonderung des Magensaftes geschieht bei diesem Hunde ununterbrochen. Beim Kauen des Fleisches wird die Sekretion um mehrere Male verstärkt; Atropin hebt sie auf. Wenn man die Pfote dieses Hundes in eisiges Wasser taucht, so verbleibt sie dort unbestimmt lange Zeit.

In dieser Weise sind die Geschmacks-, Taktil- und die Temperaturreflexe bei diesem Hunde in einem bedeutend schlimmeren Zustande, als bei anderen beschriebenen Hunden ohne Grosshirn (G. Zeliony).¹

¹ G. Zeliony. Der Hund ohne Grosshirn. "Berichte der Petersburger Gesellschaft russischer Aerzte (russisch) 1911-12." "Compt. rend. Soc. Biolog." 1913; "Communic. to the XI Intern. Physiol. Congress" 1923; "Presse médicale" 1926, No. 26; "Revue de Médecine" 1929.

Ein Jagdpfeifen oder andere starke Laute riefen die ersten 3 Monate (nach letzte Operation) ein Spitzten der Ohren, ein Bewegen des Kopfes und manchmal ein Abschütteln des Halses und des vorderen Körperteils und ein Versuch mit der Hinterpfote das Ohr zu kratzen hervor. Es gelang oft durch Laute ein Abschütteln hervorzurufen, wenn man vorläufig mit den Händen den Hals des Hundes umfasste. Das Gewinsel anderer Hunde wurde manchmal von diesem Hunde mit einem Entgegengewinsel beantwortet. Wenn man irgend einen Laut 20–30 Mal nach einander wiederholte, so hörte das Spitzten der Ohren auf, während andere Laute diese Tätigkeit nicht einbüßten. Folglich unterscheidet der Hund verschiedene Laute.

Im 3-ten Monate wurde ein Versuch gemacht bedingte Reflexe auszubilden. Zu diesem Zwecke wurden die Schläge des Metronoms mit einer starken Reizung der linken Vorderpfote durch elektrischen Strom kombiniert. Der bedingte Reflex (Heben der linken Pfote) auf den Schlag des Metronoms bildete sich jedoch nicht aus. Darauf wurde das Metronom durch eine Jagdpfeife ersetzt, und nach 103 Kombinationen (nach 4 Monat. nach Operation) rief letztere beständig ein Heben der Linken Vorderpfote und, öfters, ein Zurückweichen des Hundes hervor. Andere Laute von ungefähr derselben Stärke hatten ebenfalls ein Heben der Pfote, jedoch ein weniger Ausgesprochenes, zur Folge. Parallel mit der Entwicklung der geschilderten assoziativen Reaktion hörten die Laute auf ein Spitzten der Ohren hervorzurufen.

PONIROWSKY, NICOLAUS und WERA ISCHUNINA (CHARKOW). Die Endokrinen Organe und der Verdauungsapparat.

Die Frage über den Einfluss der endokrinen Drüsen auf die Funktion des Verdauungsapparates stellen wir im Zusammenhang mit dem allgemeinen Thema, das von der Abteilung für Physiologie des Ukrainisch. Psychoneurologischen Institutes und dem physiologischen Laboratorium des staatlichen Veterinär-Institutes zu Charkow über die Wirkung der Hormone auf die vom vegetativen Nervensystem innervierten Organe ausgearbeitet wird.

Der Einfluss der endokrinen Drüsen auf den Verdauungsapparat ist bisher wenig erforscht; doch zeugen schon die bisherigen verhältnismässig wenigen Untersuchungen sowohl klinischen wie experimentellen Charakters (Literatur: *Biedl, Bauer, Curschmann, Chvostec, Grote, Orlow, Boenheim, Badylkes, Hess u. Hundlach, Rogers, Rahe, Fawcett u. Hackett, Alpern, Predtetschensky u.m.a.*) von der grossen Bedeutung der innersekretorischen Organe für die motorischen und chemischen Funktionen des Magen-darmtraktes.

Dies zwingt uns zu einer allseitigen Untersuchung über den Einfluss der endokrinen Organe auf die Tätigkeit des Verdauungsapparates.

Diese Mitteilung hat das Ziel—die sechs-jährige Arbeit mehrerer unserer Mitarbeiter (*Schazillo, Babitschew, Berenstein, Kogan, Askalonow, Tschernjawsky, Raysky, Lubimow, Kamenew, Mantz, Aisenmann u.a.*) zu umfassen.

Unsere Versuche wurden an Hunden mit chronischen Fisteln der Verdauungsdrüsen nach *Pawlow* angestellt.

Die Resultate unserer Untersuchungen waren:

1. Die intravenöse Einführung von Pituitrin ruft eine deutliche hem-

mende Wirkung auf die Sekretion des Speichels und auf die periodische Sekretion des Darmsaftes hervor.

Pituitrin kann überhaupt als hemmendes Hormon für die Verdauungsdrüsen angesehen werden, das (nach den Angaben aus der Literatur zu schliessen) besonders hemmend auf die Magendrüsen wirkt und auf die Speicheldrüsen (unsere Beobachtungen), und weiter auch auf die Darmdrüsen; bei wiederholter Injektion selbst kleiner Pituitrindosen geben aber auch letztere das Bild ganz deutlicher Hemmung ihrer Tätigkeit.

2. Angriffspunkt der hemmenden Wirkung des Pituitrins ist nicht das Zentralnervensystem, sondern das drüsige Organ selbst, da die Sekretionsverminderung der Speicheldrüsen sowohl nach teilweiser (Chordadurchschneidung) wie auch nach vollständiger Denervation der Drüse (Durchschneidung von Chorda und sympathischem Nerv) auftritt.

3. Die hemmende Wirkung des Pituitrins auf die Drüsensekretion ist besonders deutlich bei der Pilokarpin-Speichelabsonderung, viel geringer bei der Physostigmin-Speichelsekretion (bei einem vorher atropinisierten Tiere) und fehlt gänzlich bei Adrenalinsalivation (im Falle, dass vollständig reines sympathisches Sekret erhalten wird, d.h. nach Atropinisierung des Tieres oder nach Chordadurchschneidung).

4. Die besonders deutliche Verminderung der Speichelsekretion bei Reizung (mit Pilokarpin) der parasympathischen Nerven, d.h. jener Nn., welche hauptsächlich die Wasser- und möglicherweise auch die Salzabsonderung regeln, zwingt zur Annahme, dass die Pituitrinwirkung auf die Drüsen hauptsächlich auf die Veränderung ihres Wasser-Stoffwechsels gerichtet ist.

5. Subkutane Injektionen grosser und intravenöse Injektionen mittlerer Adrenalindosen geben sehr häufig am nächsten Tage nach der Einspritzung eine Erhöhung der Speichelsekretion bei der Fütterung des Tieres, wobei die mit dem Speichel ausgeschiedenen festen Bestandteile vermehrt sind, wie ja zu erwarten war. Grosse Adrenalindosen setzen jedoch bei ihrer intravenösen Einführung gegen das Ende zu die Sekretion des Speichels unter denselben Bedingungen, d.h. am nächsten Tage nach der Injektion etwas herab.

6. Die erwähnte günstige Wirkung bestimmter Adrenalindosen auf die sekretorische Tätigkeit der Drüsen findet möglicherweise in einer spezifischen Wirkung des Adrenalins auf die trophischen Nerven des Organes ihre Erklärung. Die Frage der Möglichkeit einer solchen Adrenalinwirkung verdient unserer Meinung nach grösste Aufmerksamkeit und gründliche Untersuchung.

7. Die vorangehende Atropinisation des Tieres Evrmindert, wenn auch nicht gänzlich, so doch um ein Vielfaches die durch Adrenalin erzeugte Salivation, wenn man sie mit den Zahlen vergleicht, die das Adrenalin bei normalen Tieren gibt. Die Menge der festen Bestandteile steigt hierbei beträchtlich an.

8. Das gleiche Resultat wie bei der Atropinisierung erhält man bei Adrenalininjektion an Tieren mit denervierter Drüse. Daraus folgt, dass der Speichel, der bei normalen Tieren auf Adrenalin gewöhnlich in so grosser Menge erhalten wird, grösstenteils als cerebraler Speichel und ausserdem von zentraler Herkunft erscheint. Daraus können wir den Schluss ziehen, dass die Verminderung der durch Adrenalin hervorgerufenen Salivation nach Atropin nicht infolge Lähmung des sympathischen Nerven

oder der sekretorischen Zellen durch dieses letztere hervorgerufen wird, sonderen als Resultat der durch das Atropin verhinderten Übergabe der vom Zentrum kommenden Reizung anzusehen ist.

9. Insulin in kleinen, nicht toxischen Dosen ruft keine Speichelsekretion hervor. Grosse (toxische) Insulinmengen rufen an und für sich eine starke Salivation hervor.

10. Geringe Insulindosen, welche die durch Adrenalin hervorgerufene Speichelsekretion bloss hemmen, aber selbst eine Salivation nicht hervorgerufen und auf die Versuchstiere keine toxische Wirkung ausüben, erhöhen die durch Pilokarpin erzeugte Salivation und können selbst toxische Wirkung zeigen, indem sie Erbrechen und Zittern des ganzen Körpers auslösen.

11. Der auf grosse Insulindosen hin erhaltene Speichel und ebenso der nach Punkt No. 10 nach Pilokarpinverabreichung erhaltene, ist seinen Eigenschaften nach ein rein cerebraler Speichel, während das auf Adrenalin hin gewonnene Sekret der Speicheldrüsen (eines ebenfalls pilokarpinisierten Tieres) dem sympathischen Speichel nahesteht.

12. Die angeführten Beobachtungen und ebenso solche an Tieren mit denervierten Speicheldrüsen erlauben uns den Schluss zu ziehen, dass das Insulin in gewissem Grade den Angriffspunkt seiner Wirkung an den peripheren Endungen des parasympathischen Nervensystem hat. Die Wirkung des Insulins auf die Brech- und Krampfbereiche jedoch zu einer Zeit, wo das Erbrechen noch nicht auf Hypoglykämie zurückgeführt werden kann, und ebenso der Umstand, dass die Vermehrung der Pilokarpinsalivation an Drüsen mit ganzen cerebralen Nerven stärker ist, als an denervierten Drüsen, sprechen dafür, dass das Insulin, besonders in grösseren Dosen, weitaus nicht gleichgültig sich dem Zentralnervensystem gegenüber verhält.

13. Intravenöse Injektionen nicht zu grosser Dosen von (1-2 cem) Spermol oder Ovarin verstärken nicht die Speichelabsonderung, bei Erhöhung der Dosis aber tritt eine solche in mehr oder minder ausgesprochenem Masse auf. In diesem Falle ist das Auftreten der Salivation am wahrscheinlichsten auf eine beginnende toxische Wirkung der erwähnten Präparate auf das Zentralnervensystem überhaupt zurückzuführen, da sie bei Atropinisierung des Tieres nicht auftritt und mit dem Zustande der Erregung des Tieres und der auf ihn folgenden Depression und ebenso auch mit anderen Erscheinungen von Seiten der Gehirnzentren zusammenfällt.

14. Intravenöse Injektionen von Spermol (1-2 cem) erniedrigen nur in unbedeutendem Ausmasse die durch Fütterung und Pilokarpin hervorgerufene Speichelabsonderung; die hemmende Wirkung des Spermols auf die durch Adrenalin erzeugte Speichelsekretion hingegen ist deutlicher ausgesprochen (die Erniedrigung beträgt bis zu 20-40 Prozent.)

15. Intravenöse Injektionen von Ovarin (1-2 cem) setzen die durch Fütterung und Pilokarpin hervorgerufene Speichelabsonderung etwas stärker herab als Spermol; die durch Adrenalin erzeugte Salivation aber wird durch Ovarin sehr stark gehemmt (bis 75-80 Prozent). In letzterem Falle erinnert das Ovarin sehr stark an das Insulin, das die Adrenalin-Salivation ebenfalls stark herabsetzt oder ihr Auftreten selbst verhindert.

16. Die eben erwähnte Wirkung des Spermols und Ovarins auf die Speichelsekretion, besonders auf die nach Adrenalin, erlaubt in ihnen Antagonisten des Thyreoidins zu sehen, das die Speichelabsonderung er-

höht, und sie als Synergisten des Insulins aufzufassen, das noch stärker als sie durch Adrenalin hervorgerufene Speichelsekretion herabsetzt.

17. Die Schilddrüse besitzt eine grosse Bedeutung für die Arbeit der Verdauungsdrüsen. Ihre Entfernung aus dem Organismus setzt die Sekretion des Magensaftes herab, ihre Extrakte vermehren die Sekretion von Magensaft und Speichel.

18. Nach Entfernung der Epithelkörperchen ist vor dem Eintritt völliger Tetanie die Speichelsekretion auf Pilokarpin erhöht, auf Adrenalin herabgesetzt; bei stark ausgesprochenen Tetanie, beim Eintritt allgemeiner Kachexie, ist die Speichelsekretion vermindert.

19. Die K- und Ca-Salze spielen offenbar eine wichtige Rolle, nicht nur in der Funktion der Muskelorgane, sondern auch bei den Verrichtungen der Drüsenebile.

PORTER, EUGENE L. (GALVESTON). **Evidence That the Postural Tonus of Decerebrate Rigidity Increases in Amount by the Successive Innervation of Single Motor Neurones.**

The author has previously published evidence that the flexion reflex in the spinal cat, when elicited by single shocks of increasing strength applied to a sensory nerve increases in amplitude by discontinuous steps of an all-or-none character. The evidence indicated that each step represented the activity of an additional motor neurone and the muscle fibers innervated by it.

The present investigation was undertaken to see if the tonic contraction of decerebrate rigidity also increases by discontinuous steps according to the same principle.

The phenomenon in spinal reflexes is seen only when the record of contraction is taken from a very small muscle such as the tenuissimus. In the present research a minute portion of a tail muscle—the extensor caudae lateralis—has been employed. The muscle as a whole is made up of a series of small muscles, each with its own tendon. That portion attached to a single tendon has been used.

This muscle is involved in the characteristic rigidity which develops in a decerebrate cat. It may show spontaneous changes in tonus or it may be necessary to elicit these by artificial stimulation, as by rubbing the tail fur the wrong way or by dorsi-flexing the neck.

When from any cause the muscle passes from rest into tonic contraction the record shows a series of sharp steps, never a smooth and uniform increase in height.

If, now, the muscle is used as a nerve-muscle preparation and the motor nerve stimulated by single shocks of gradually increasing strength, the response of the muscle is by contractions occurring in step-like groups with no gradation between the successive groups. Each group or step represents presumably the activity of a single motor neurone and the muscle fibers innervated by it, as in the case of tenuissimus in the spinal flexion reflex.

The tonic contraction steps are often of almost exactly the same height as the nerve-muscle steps from the same muscle, and are always of the same order of magnitude. They have an all-or-none character.

These results indicate that the tonic contraction of decerebrate rigidity increases in amount by the innervation of one motor neurone after another

with the resulting contraction of the muscle fibers innervated by each neurone.

In this respect tonic contraction in the decerebrate animal resembles ordinary reflex contraction in the spinal animal.

PORTER, EUGENE L. (GALVESTON). **Method of Using a Small Tail Muscle of the Decerebrate Cat for the Study of Postural Tonic Contraction. (Demonstration)**

PORTER, W. T. (BOSTON). **An Electric Kymograph. (Demonstration)**

POULTON, E. P. and J. W. SHACKLE (LONDON). **Two Simple Apparatuses for Determining Roughly the Oxygen and CO₂ Content of A Gaseous Mixture.**

PRATT, FREDERICK H. and MARION A. REID (BOSTON). **An Examination of Apparent Exceptions to the All-or-Nothing Law.**

The branching striated fibers of the lymph hearts and of the retrolingual membrane (membrana basihyoidea) in the frog, are known to be activated by somatic nerves, which in the case of the lymph hearts convey independently rhythmic impulses from spinal cells. In both, moreover, direct and indirect excitation, as heretofore applied, has elicited graded response to graded stimuli, thus seeming to place these tissues outside the jurisdiction of the all-or-nothing law. Photographic records (from *R. pipiens* with intact circulation) by the mercury droplet method and with sharply localized micro-electrode stimulation, reveal however the same discontinuities found in skeletal muscle, with all-or-nothing response within a certain range of stimuli. In the retrolingual membrane, with graded excitation of an individual fiber, the responses are of uniform minimal value. Both structures therefore display fractional contraction, which must involve limited areas of interconductance in an apparent syncytium.

PRATT, FREDERICK H. (BOSTON). **Apparatus for Observing and Recording Movements of Single Muscle Fibers. (Demonstration)**

PUCHE-ALVAREZ, J. (BARCELONA). **Asphyxia as an Agent of Hypoglycemia.**

The action of asphyxia as a stimulus to hyperglycemia is well known. Macleod and McCormick, Stewart and Rogoff consider this way of producing hyperglycemia to be the most efficient one, and think it may serve as a standard procedure with which to evaluate the other experimental methods of producing hyperglycemia. The mechanism through which this effect is produced appears definitely to involve a double mechanism, both humoral and nervous. The nervous effects are conveyed to the effector organs through the splanchnic nerves.

My experiments had the purpose of determining what would happen to the blood sugar after interrupting the continuity of the splanchnics.

A. I determined the effect of asphyxia on the blood sugar of dogs under fasting conditions, anaesthetized by chloralose and after sectioning the splanchnics in the thorax. Under these conditions asphyxia produces a lowering of the blood sugar manifested 15 to 60 minutes after the stimulus.

B. In another series I performed hepatic denervation. This intervention did not alter the hypoglycemic effect of asphyxia.

C. To exclude the cardiac agent (asphyxial bradycardia) I sectioned, in another group of experiments, the pneumogastric fibres which lead to the heart. Under these conditions, asphyxia produced also hypoglycemia.

D. To find out whether the asphyxial stimulus liberated some substance of pancreatic origin, I used the method of the jugular-pancreatic anastomosis (La Barre), joining the pancreatic vein of a given dog (submitted to splanchnicotomy and asphyxial stimulation) with the jugular of another dog in a fasting condition anaesthetized with chloralose. I was able to determine in a certain number of experiments the hypoglycemic effect thus transmitted by humoral means.

E. The section of the splanchnics in the receiving dog makes the hypoglycemic effect longer than in dogs with intact splanchnics.

The determinations of blood sugar were made after the method of Hagedorn-Jensen. Asphyxia was produced by obstruction of the trachea for periods of 1 minute, with intervals of 1 to 2 minutes. In the experiments of anastomosis, pancreatic blood was allowed to pass during 15 minutes.

From these facts and from a few new ones that I have observed after the present abstract was written, I conclude that asphyxia, after occlusion of the hepato adrenal nerve paths, is the cause of a lowering of blood sugar from vagal pancreatic stimulation.

PUTZEYS, PAUL (LOUVAIN). On the Ionization of Proteins.

A method whose principle has been often used for various purposes, has been subjected to a critical experimental investigation and perfected in order to adapt it to the determination of the mean value of the number of charges carried by a protein ion. It consists in the measurement of: 1, the amount of protein ions which have travelled from one compartment of the apparatus to another;—2, the amount of oppositely charged ions which have moved in the opposite way and whose charge is known; 3, the total amount of electricity transferred by the two ion species as measured by a coulometer. The charge of the transferred amount of protein is then given by the difference between 3 and 2. The special features, the improvements of the technic, the errors, the corrections and the accuracy of the method are discussed.

Preliminary results for ovalbumin are given.

QUAGLIARIELLO, G. (NAPLES). Contenuto in Na, K, Ca e Mg del succo muscolare e del suo ultrafiltrato.

Muscoli di cane uccisi per dissanguamento, liberati nel miglior modo possibile del connettivo e del grasso interstiziale, tritati a macchina e pestati con sabbia di quarzo, pura all'analisi, sono stati pressati al torchio idraulico sino alla pressione di 250 atmosfere. In una parte del succo muscolare (pH circa 6) si sono determinate le sostanze proteiche, il residuo secco a 110°C. e le ceneri. Un'altra parte del succo, circa 300 cmc, è stata ultrafiltrata attraverso membrana di collodio acetico 10%. I primi 10 cmc di ultrafiltrato sono scartati e si raccolgono i successivi 30-35 cmc che vengono portati a secchezza e inceneriti.

Sulle ceneri del succo intero e dell'ultrafiltrato si determina il Na, il K, il Ca e il Mg.

Nella soluzione delle ceneri, dopo aver allontanato i fosfati ed i metalli dei primi quattro gruppi analitici, si precipita il Ca come ossalato e il Mg come carbonato e l'uno e l'altro vengono determinati come ossidi. Il K e il Na si determinano globalmente come cloruri, e il K poi come cloro-platinato, ottenendo per differenza il Na.

I risultati delle analisi sono i seguenti:

	Na	K	Ca	Mg
In 100 g. di succo intero, g.	0,0460	0,4310	0,0347	0,0712
Nell'ultrafiltrato di 100 g. di succo, g.	0,0470	0,2860	0,0195	0,0308
Differenza, g.	-0,001	+0,1450	+0,0152	+0,0404

Da questi dati risulta che circa 1/3 del K e i 2/5 del Ca e del Mg si trovano nel succo muscolare in una forma non ultrafiltrabile.

Per quanto è a mia conoscenza, non esistono in letteratura dati sullo stato di questi elementi nel muscolo cui possano essere riferiti questi dati ottenuti nel succo, meno che per il K, una parte del quale, secondo Neuschlosz, si trova nel muscolo in una forma non diffusibile, cosa per altro negata da Höber. Se consideriamo invece lo stato di questi elementi nel plasma del sangue, troviamo che mentre il K è tutto o quasi ultrafiltrabile, una buona parte del Mg e una parte anche maggiore del Ca non lo sono. E' evidente che questi elementi, nel muscolo come nel plasma, si trovano in qualche modo fissati ai colloidi.

QUIGLEY, J. P. and A. J. CARLSON (CHICAGO). The Influence of Insulin on the Motility of the Gastro-Intestinal Tract.

Gastric activity in normal men was recorded by the triple balloon method. In men fasting from 15-44 hours, 8-20 units of insulin produce a gastric response in 40-90 minutes. The response consists of 1, a rise in tone; 2, a series of rapidly repeated contractions (usually most marked in the pyloric end of the stomach); 3, an unusually prolonged hunger period (continuous activity lasting five hours has been recorded). This activity is not depressed by smoking, mild nausea, pleasant or unpleasant emotions, bodily discomfort, taking food into the mouth or even the introduction of 100 grams of cane sugar, 18 grams dextrose and 250 cc. of water into the stomach. The activity is promptly inhibited by the introduction of cane sugar or dextrose into the duodenum or by the subcutaneous injection of atropine (0.5 mgm.) or epinephrin (0.5 mgm.). With each of these procedures a direct relationship was observed between gastric motility and hunger sensations.

Using two balloons in the duodenum and a balloon in the stomach it was demonstrated in man that duodenal activity induced by insulin parallels that noted in the stomach. As in the stomach, duodenal activity is inhibited by cane sugar introduced into the duodenum or by the subcutaneous injection of atropine.

In normal dogs the gastric motility induced by insulin is likewise inhibited by the subcutaneous administration of atropine or epinephrin. In dogs with a Heidenhain pouch, insulin produces a decrease in motility of the pouch which parallels the increase in activity of the main stomach.

Frequently the activity of the pouch can be increased by the intravenous injection of dextrose while the main stomach is showing depression.

In dogs having the vagi sectioned above the diaphragm insulin produces a depression of gastric motility. A pouch made of the pyloric end of the stomach (vagus fibers sectioned) failed to respond to insulin. Motility of the dog's colon as recorded by a balloon introduced through a cecal fistula was increased by insulin and decreased by intravenous injection of dextrose in a manner similar to the normal stomach.

RAAB, W. (VIENNA and PRAGUE). Hyperexcitability of Vasomotor Centers to CO₂ Tension as a Pathogenetic Factor in Essential Hypertension.

Slow deep breathing decreases the systolic blood pressure of patients suffering from essential hypertension without exception (within 15 minutes a fall in pressure averaging 28 mm. with a maximum of 60 mm.). In healthy persons this practically does not occur. The loss of CO₂ from the alveolar air (*i.e.*, from the arterial blood) has no distinct influence upon the blood pressures of normal individuals whereas in hypertonic patients the CO₂ curve and the blood pressure curve both sink parallelly and after stopping the deep breathing both rise up quickly again. Deep breathing with a gas mixture containing 3 per cent CO₂ and 97 per cent oxygen prevents the decrease of CO₂ in alveolar air as well as the fall in blood pressure. Thus the decrease of blood pressure during deep breathing is not a mechanical effect but due to the loss of CO₂. CO₂ inhalation in a closed gas-apparatus increases the blood pressure of hypertonic persons on an average 3 times the amount seen in normal individuals. The CO₂ tension of hypertonics is not higher than normal; the irritability of the respiratory center in hypertonics is not less than that of normal individuals. Thus an absolute increase of CO₂ does not occur but the pathological hyperirritability of the vasomotor centers is an important factor in the increase of blood pressure present in the hypertonic individuals. (It is known that CO₂ acting upon the vasomotor centers causes vasoconstriction.) Simple peripheral increase of blood pressure as produced by adrenaline injection is not at all affected by hyperventilation in normal individuals. On the other hand the peripheral vasoconstrictor effect of adrenaline and the hyperventilation effect in the central nervous system of hypertonic persons counteract each other: the adrenaline effect is masked.—In contrast to the cases of essential hypertension, patients suffering from high blood pressure secondary to nephritis, react to hyperventilation like normal individuals who have no hyperexcitable centers but who have peripheral increase of the blood pressure (see adrenaline effect above): the effect is completely lacking.—The nature of essential hypertension lies in a hyperexcitability of the vasomotor centers especially to the CO₂ tension of the blood (even in the normal physiological tension) whereas in the case of patients suffering from nephritis with high blood pressure this factor is of no practical importance.

RABBENO, A. (PAVIA). Sull'azione farmacologica del pirrolo e di alcuni suoi derivati.

Si è indagata l'azione del pirrolo e dei pirrilalchil (aril) chetoni α -sostituiti (acetil-propionil-butiril-benzoilpirrolo) nella rana e nel coniglio. Nella rana il pirrolo provoca paralisi centrale discendente e contrattura muscolare

riflessa. Negli effetti dei *chetoni pirrolici* si può riconoscere la doppia azione propria del pirrolo; ma mentre in questo paralisi centrale e contrattura muscolare sono sullo stesso piano, nei derivati chetonici è esaltata la componente narcotica mentre è attenuata od abolita quella convulsivante, la quale però nel propionil e nel butirrilpirrolo, con dosi molto elevate, letali, giunge a provocare un vivace accesso contrattorio, tonico, riflesso, che si risolve coll'instaurarsi della paralisi.

Sul cuore isolato si osserva cronotropismo ed inotropismo negativo che giunge sino all'arresto diastolico. Sul sistema nervoso isolato (preparato anteriore dell'Herlitzka) il pirrolo ed i suoi chetoni, aboliscono l'eccitabilità riflessa; ma mentre nella perfusione del preparato anteriore, i riflessi midollari scompaiono prima dei corticali, nella rana in toto l'eccitabilità del cervello precede quella del midollo. Il preparato anteriore si dimostra un reattivo biologico molto più sensibile del cuore isolato, all'azione narcotica dei chetoni pirrolici e permette di determinare la concentrazione minima narcotica di ciascun termine, con approssimazione nella seconda cifra significativa; sul cuore bisogna accontentarsi della prima.

Un periodo di esaltata eccitabilità riflessa precede, nella rana, la narcosi; concentrazioni debolissime ($1/3-1/30$ della minima narcotica) aumentano il tempo di sopravvivenza del preparato anteriore; forti diluzioni dimostrano inotropismo positivo sul cuore; vale perciò per pirrolo e chetoni pirrolici la regola generale: in piccole dosi esaltano, in dosi elevate deprimono l'attività degli organi. *Azione anestetica locale.* I diagrammi ottenuti fanno rilevare che ad una concentrazione grandissima (soluzione satura) corrisponde un tempo minimo di anestesia locale nullo; ad un tempo minimo infinito una concentrazione nulla. Sugli organi isolati l'azione è perfettamente reversibile.

Quantitativamente l'attività tossica e narcotica aumenta dal pirrolo al primo, secondo, terzo termine alifatico per raggiungere il valore più alto nel derivato fenilico. Ad es.: la tossicità lontana (rana in toto) cresce come 1:1,4:2,7:5,1:13,8; l'attività sul cuore isolato come 1:2:4:10:30; l'attività narcotica sul sistema nervoso isolato come 1:1,3:4,9:21:73. Per i termini alifatici (*acetil-propionil-butirrilpirrolo*) nella rana l'attività tossica procede come 1:2:4 ($Q = 2$); l'attività narcotica come 1:5:10; ($Q = 3,3$); sul cuore isolato 1:2:5 ($Q = 2,25$); sul sistema nervoso isolato 1:4:8 ($Q = 4$). In generale si può dire che l'attività dei chetoni pirrolici aumenta secondo una funzione esponenziale; varia il quoziente che è uguale a 2 per l'attività tossica (cuore) a 3 o 4 per l'attività narcotica (sistema nervoso).

Sul coniglio (normale e iperpiretico) questi farmaci abbassano notevolmente la temperatura del corpo. L'azione antitermica per il benzoilpirrolo è superiore, ma meno prolungata, per l'acetilpirrolo è inferiore a quella dello stesso pirrolo. Nell'acetil e propionilpirrolo accanto all'azione antipiretica si manifesta una depressione dell'eccitabilità cerebrale che può giungere a temporanea abolizione dei riflessi midollari con conservazione di quello corneale; quest'azione narcotica compare solo con dosi superiori alle minime antitermiche. Gli effetti sul coniglio del butirril, benzoilpirrolo e dello stesso pirrolo, si riducono a quelli sulla temperatura. La tossicità del pirrolo è relativamente elevata (0.0022 g mol per Kg, per via gastrica); i chetoni pirrolici invece, anche in dose doppia, sono innocui, mentre presentano potere antitermico non inferiore a quello dell'acetanilide, piramidone, aspirina, di cui sono meno tossici.

Nella rana i chetoni pirrolici agiscono quali narcotici convulsivanti ed anestetici locali; nel coniglio quali antipiretici.

RANDOIN, LUCIE (PARIS). **Équilibre alimentaire et nutrition.**

Vers 1922, Mme L. Randoïn, à la suite d'observations relatives aux effets d'une avitaminose déterminée ou d'une carence minérale spéciale, a été amenée à penser, en collaboration avec H. Simonnet, que le principe de l'isodynamie devait se trouver limité, d'une manière assez étroite, par les variations quantitatives de certaines vitamines ou de certains éléments minéraux, et que, pour assurer à l'organisme une nutrition parfaite, il fallait tenir compte de rapports nécessaires entre les matières énergétiques et les substances non énergétiques des régimes.

Dès lors, Mme L. Randoïn s'est appliquée à rechercher le rôle possible des corps spécifiquement indispensables (éléments minéraux et acides aminés indispensables, vitamines) dans l'utilisation, par l'organisme, des substances énergétiques, ainsi que les équilibres alimentaires les plus satisfaisants dans certains cas physiologiques déterminés.

1°. Mme L. Randoïn, en collaboration avec H. Simonnet, a démontré, en 1923-1924, qu'une ration renfermant l'énergie potentielle nécessaire à un organisme n'entretient celui-ci (ou ne permet sa croissance) que si le rapport $\frac{\text{vitamines B}}{\text{glucides}}$ ne descend pas au-dessous d'une certaine valeur.

Des troubles éclatent, soit lorsqu'on augmente suffisamment la proportion des glucides d'une ration, soit quand on diminue la proportion des vitamines B. Des deux manières, on produit un déséquilibre.

2°. Mme L. Randoïn, en collaboration avec J. Alquier, a prouvé, en 1925-1926, la nécessité d'un équilibre déterminé entre les composants minéraux et les composants énergétiques des régimes, aussi bien pour le développement de l'organisme que pour l'accomplissement des fonctions de reproduction. Ces auteurs ont montré qu'une ration satisfaisante se trouve déséquilibrée, soit par un apport de sels minéraux, soit par un supplément de glucides, mais non par un apport simultané de ces deux sortes de substances, en proportions convenables.

3°. Enfin, les années suivantes, (1927-1929), Mme. L. Randoïn, en collaboration avec R. Lecoq, après avoir établi qu'avec des régimes artificiels (*exclusivement privés de vitamines B*) renfermant 66 p. 100 de galactose ou 66 p. 100 de lactose, l'emploi quotidien d'une forte dose de levure de bière n'empêche ni les accidents nerveux ni la mort du Pigeon (au bout de 15 à 30 jours), a montré ensuite qu'en modifiant les proportions des substances énergétiques, on peut arriver à obtenir un équilibre alimentaire beaucoup plus satisfaisant.

Par exemple, en employant un régime artificiel de composition analogue à celle du lait desséché (renfermant 35 p. 100 de lactose, seulement) l'addition quotidienne de 0 gr. 20 de levure de bière permet une survie de 90 jours et celle de 0 gr. 50 le levure de bière, une survie d'environ 150 jours. (*Laboratoire de Physiologie du Centre de Recherches sur l'Alimentation. Institut des Recherches Agronomiques—Paris—France.*)

RAPPORT, DAVID (CLEVELAND). **The Utilization of the "Waste Heat" of Metabolism in Muscular Exercise.**

In view of the fact that the energy for recovery from exercise can appar-

ently be derived from the oxidation of fat as well as of carbohydrate, implying that the exothermic portion of this recovery is non-specific, experiments were carried out to see whether what is ordinarily waste heat, such as the specific dynamic action of foodstuffs, can also act as a source of free energy for this purpose. In the present experiments an animal, after being given fat, glucose, or meat, was caused to run about two hours later on a horizontal treadmill introduced into a closed system for measuring the gaseous exchange. The excess metabolism of exercise and recovery, and the number of calories required to do 1 "horizontal kilogrammeter" of work, were calculated, and these were compared with the similar results obtained when the animal was in the post-absorptive condition. It was found that in the latter case 2.40 cal. were needed to do 1 "horizontal kilogrammeter" of work. When fat was given, the average of the resting metabolism before and after exercise was elevated 20 per cent; but the animal needed only 5.8 per cent more energy to do work than in the post-absorptive condition (2.54 cal. per kgm-m. of work), indicating an almost complete abolition of the specific dynamic action. The same thing held true for glucose, the energy consumption in work being practically the same (2.38 cal. per kgm-m. of work) as when the animal had had no food. This latter result confirms the observation of Anderson and Lusk (1917) with respect to glucose, these observers noting an actual decrease of 5 per cent in the energy requirement for exercise after glucose ingestion. When meat was administered, however, the specific dynamic action and the work metabolism were summated, as Rubner had originally shown.

In another series of experiments, 0.1 gram of epinephrin per kilo was injected subcutaneously, showing an average increase of the resting metabolism above the basal level amounting to 42 per cent. Upon exercise, this increase was summated with that of work, for 55 per cent more energy was needed to perform exercise than when epinephrin was not injected. A similar result was obtained with tyrosine, the specific dynamic action of 18 per cent being completely summated with the excess metabolism of exercise.

It appears, therefore, that in some cases the "waste heat" of metabolism can be utilized by the body as free energy, as in the case of the specific dynamic action of fat and carbohydrate: but not in others, as in the case of meat protein and tyrosine specific dynamic action or the "calorigenic" action of epinephrin, which in this respect behaves like an amino acid. This last point is particularly interesting in view of the putative origin of epinephrin.

RASENKOV, I. P. (Moscow). The Influence of High Temperatures on the Organism of Animals.

Summary report of the work of A. H. Petrachev, E. B. Babsky, G. U. Grönberg, M. L. Idinova, A. M. Blinova, H. S. Koshtoyanz, O. F. Zavali-shina, G. V. Derviss, E. F. Georgievskaya, E. A. Kafieva, A. G. Kozlova, A. V. Lyzlova, S. E. Severin, A. N. Kafanov.

(The object of the study was to determine the influence of temperature, single and repeated application, at 30°, 40°, 50°, 60°C. and with a relative or absolute humidity in a specially constructed chamber) Observations were made on: the secretion of saliva, intestinal secretion, gastric secretion, periodic contraction of the stomach, reserve energy of the

heart, blood pressure, rate of the blood flow, blood composition and glycogen of the liver.

Secretion of saliva at 40°C. was observed during 2-6 hours to be of an equal rate and unchanged in composition. At 50°C. the amount of saliva increases.

Intestinal secretion called forth by a mechanical stimulus does not change when the animal is kept at high temperature. *Periodic secretion:* During 2-3 hours after heating an increase in length of the periods of work or their total disappearance can be observed. Then commences a prolonged increase of periodic intestinal secretion. These phenomena are distinctly noticeable at 50°C.; at 40°C. they are weaker and at 30°C. they are absent. The content of kinase and lipase remains unchanged.

Gastric secretion: Keeping the animal at 30°C. and at an absolute humidity of 32 mm. for 45 minutes produces an increased gastric secretion without any special changes in acidity and digestive capacity. At 40°C. no changes are observed, at 50°C. there is a decrease in the amount of gastric juice, a decrease, or disappearance, of the reflex phase, a decrease of the chemical phase, a shortening of the periods of secretion, decrease in acidity and an increase in the digestive capacity.

Periodic contractions of the stomach: On keeping the animal for 2-4 hours at a temperature of 40°C. and at 32 mm. of relative humidity, a small increase in the period of rest and a shortening of the period of work is observed. On keeping the animal 1-1½ hours at a temperature of 50°C. and the same humidity, a distinct diminishing of the periodic activity takes place.

Heart-blood vessel system: On placing the animal into a chamber of a temperature of 50° and with an absolute humidity of 29 mm. at first the arterial pressure remains at the same level, the contractions of the heart increase, respiration becomes more frequent, the vasomotor response of the N. femor. to the electric current is normal, the rate of the blood flow increases. Then the blood pressure begins to drop (usually with the temperature of the body higher than 42°) the frequency of the contractions of the heart increases, the blood flow decreases, respiration becomes less frequent. The vasomotor response to stimulation of the N. femor. is absent in the majority of cases. On continuing to increase the heating the respiration stops and in some seconds the heart stops also. On cutting the two vagi stopping of the heart is observed before respiration ceases. Spinal transection does not change the results of overheating.

On prolonged heating (from 1-2½ months) the reserve energy of the heart decreases.

The blood composition: On keeping the animal 1 hour in a chamber at 30°C. and at an absolute humidity of 29 mm. no changes occur.

At 40°C. and the same humidity as above the body temperature increases to 40°C. and the frequency of respiration to 80-180 per minute; an increase of lactic acid and decrease of blood sugar is also noticed.

At 50° which calls forth an increase of the body temperature to 42°C. and a rate of respiration of 250 per minute the following changes were observed:

- a. The specific gravity of the blood increased, the amount of solid residue, of the residue of nitrogen, urine and lactic acid increased also.
- b. Non-organic phosphorus, sugar and chloride decreased.
- c. An acute fall in the total quantity of CO₂ and CO₂ capacity is noticed.

d. The concentration of hydrogen ions and the CO_2 tension in the arterial and venous blood do not change significantly, while the CO_2 tension has a tendency to decrease.

e. The degree of oxygen saturation of the blood and the O_2 capacity of the arterial and venous blood change in a reverse direction.

f. The blood-oxygen capacity in the venous blood increases and in the arterial decreases.

At 60°C . the changes are more acute than at 50° .

Cerebro-spinal fluid: While heating at 50°C . for $1\frac{1}{2}$ hours the following changes are observed: pH increases, the total amount of CO_2 shows an acute drop, and the amount of lactic acid increases considerably.

RASENKOV, I. P. (MOSCOW). Influence of Qualitatively Various Food on the Functions of the Organism.

Summary report of the work of X. C. Koshtoyanz, I. M. Ivanov, E. F. Chebysheva, G. S. Ochakovskaya, I. I. Nefedova, Z. Y. Belezky, I. M. Yarmolinsky, I. P. Chukichev, O. F. Zavalishina, G. U. Grünberg, A. B. Lyzlova.

The object of the study was to determine the influence of qualitatively various food on the following: gastric secretion, periodic contractions of the stomach due to hunger, production of bile, intestinal secretion and facultative reflexes.

Gastric secretion. Under the influence of various diets the secretory activity of the gastric glands shows profound adaptive changes which result in both quantitative and qualitative changes of the gastric juice. With meat, fat, milk and liver diets as compared to the carbohydrate diet the amount of gastric juice secreted is considerably larger, with greater acidity and a larger fermentative capacity, particularly on milk and fat diets. The comparison of meat and fat diets shows that the fat diet produces a greater secretion with higher acidity but with a smaller fermentative capacity. The liver diet has a two phased action, the first one being an increase and the second a decrease of secretion. The output of secretion varies in the meat and fat diets, the reflex phase distinctly diminishes and even disappears altogether, the chemical phase increases, but the process is reversed with a carbohydrate diet—the reflex phase increases and the chemical decreases. The change in diet produces in the beginning great variations in the gastric secretion manifesting themselves in the fact that the same food stimulus calls forth at times a large amount of juice and at others a small amount of it; then in time it remains on a fixed level. The mechanism of the change of gastric secretion under various diets depends upon the accumulation of chemical stimuli in the blood, these stimuli originating from alimentary substances; if many stimuli accumulate in the blood secretion increases, if the reverse takes place, secretion decreases.

Periodic contractions of the stomach due to hunger. The above varies under the influence of various diets. With a meat diet the periods of work increase and periods of rest are prolonged. With a carbohydrate diet the inverse order takes place.

Production of bile. The production of bile on a meat diet as compared to one of oatmeal is more abundant and the secretion has a higher content of bilirubin.

Intestinal secretion. Intestinal secretion collected in response to mechanical stimuli depends also on the diet. On replacing a carbohydrate

diet by a bread-fat diet the amount of juice increases; with a change to a carbohydrate diet, however, it decreases.

Facultative reflexes. Facultative reflexes, as well as non-facultative (on a stimulus such as Zweeback powder), increase on a meat diet and decrease on a carbohydrate diet.

RAY, G. B. (CLEVELAND). **Evidence Indicating a Colorless Form of Hemoglobin.**

The following experiments are the results of observations on the changes in blood pigments of the dog following splenectomy. The total pigment concentration (everything capable of being converted to cyanhemoglobin) was measured by the colorimetric method of Stadie; functional hemoglobin was determined from the oxygen capacity. The pigments were differentiated by means of the spectrophotometer.

The following experiment is typical of the series. The difference between the hemoglobin determined from the oxygen capacity (functional pigment) and that determined by the colorimeter (total pigment) indicated that 29 per cent of the total pigment was incapable of combining with oxygen (nonfunctional pigment). The absorption curve of this blood was characteristic of oxyhemoglobin; the ratio of the extinction coefficient at 540 millimicra to that of 560 millimicra being 160. Comparison of this absorption curve with that of normal blood having the same total pigment concentration showed that the blood from the splenectomized animal had a decreased hemoglobin content. This decrease was exactly proportional to the nonfunctional pigment, a reaction found in every sample of blood examined.

These observations can only be explained by assuming that a colorless hemin derivative is formed which is capable of being converted to cyanhemoglobin by the Stadie technique.

This evidence is offered in favor of the existence of a colorless form of hemoglobin.

READ, B. E., C. PAK and B. G. ANDERSON (PEPING). **Ephedrine Compounds.**

Methyl ephedrine in the anesthetized dog in doses of 5 mgm. per kilo, slows and deepens the respiration. This is in marked contrast to ephedrine which while it may give a primary slowing has a stimulating effect producing a quicker, deeper respiration.

Methyl ephedrine compared with ephedrine has a much smaller effect upon the blood pressure. A one milligram per kilo dose may even show no effect. The pulse rate is usually slightly increased. The circulatory effects produced by methyl ephedrine are much smaller than those from ephedrine.

The stimulating respiratory effect produced by ephedrine upon a morphinized animal is not given by methyl ephedrine.

Benzyl ephedrine has been prepared. Tested by wheal anesthesia it is twice as effective as procaine. Its action is greatly potentiated by adrenaline. It shrinks the nasal mucous membranes. It is less toxic than cocaine.

REDFIELD, ALFRED C. (BOSTON). **The Absorption Spectra of Hemocyanin Solutions.**

In the absorption of light by solutions containing hemocyanin the ab-

sorption due to the prosthetic group when combined with oxygen may be distinguished from the effect due to the optical properties of the molecule as a whole.

The absorption coefficient of reduced blood of *Busycon canaliculatum*, *Limulus polyphemus*, and *Loligo pealei* varies inversely with the fourth power of the wave length as predicted by the Rayleigh theory for the scattering of light from small particles.¹ Scattering appears to account for the entire apparent absorption of these solutions. Preparations of reduced hemocyanin free of salt absorb much less light than reduced blood. Theoretically scattering at any wave length is a function only of the number and size of the particles and their index of refraction. The index of refraction is unchanged by purification;² consequently it may be deduced that in serum the hemocyanin exists in aggregates 10 or 20 times as large as in the purified preparations. The degree of aggregation appears to diminish when serum is made more alkaline (pH 9.5).

The true absorption by the oxygenated prosthetic group is obtained by correcting the spectrum of the oxygenated solution for the apparent absorption by the molecule as a whole when reduced. The spectra so obtained have a region of maximum absorption in the yellow and minimum absorption in the blue green. The relative values of the absorption coefficients for different wave lengths, on which the "shape" of the corrected absorption spectrum depends, differ very little in any one species as the result of purification. When the corrected spectra of different species are compared it is found they are strikingly alike in "shape," but differ in the wave lengths characteristic of the maximum and minimum absorption. These are approximately as follows:

	MAXIMUM ABSORPTION	MINIMUM ABSORPTION
	m μ	m μ
<i>Busycon canaliculatum</i>	565	470
<i>Homarus americana</i>	575	475
<i>Limulus polyphemus</i>	585	480
<i>Loligo pealei</i>	585	480

REED, C. I. (CHICAGO). Carbohydrate Metabolism in Parathyroidectomized Dogs.

After parathyroidectomy, there is no particular disturbance of fasting glucemia, but when such animals are in tetany, ingestion of dextrose induces a curve of tolerance characterized by a progressive increase and delayed recovery during observation periods of two to three hours. Dextrose ingestion or injection tends to alleviate symptoms of tetany, causing a decrease in inorganic phosphorus and a less pronounced decrease in calcium, thus inclining toward an increase in the calcium:phosphorus ratio.

Insulin produced, in normal and non-tetanic dogs, an increased calcemia and decreased phosphemia. When dogs were in tetany, insulin produced characteristic curves of hypoglucemia and hypophosphemia but calcemia responded much less regularly, any increase being followed by a decrease. Symptoms were usually abated following insulin administration.

¹ Rayleigh. Phil. Mag., 1899, Ser. 5, xlvii, 375.

² Quagliariello. Arch. di Sci. Biol., 1920, i, 246.

REED, C. I. and J. A. LAYMAN (CHICAGO). **Effects of Bilateral Vagotomy on Blood Pressure and Heart Rate.**

Previous observations have been extended under more carefully controlled conditions and the results in general are confirmed. Blood pressure may rise or fall after bilateral vagotomy quite independent of the effects on the heart, which suggests that the results are due to interruption of the pathway of tonic vagal impulses to the vasomotor center. Cardiac output and alterations in reaction due to slowed respiration are not responsible for the variations noted.

REHBERG, P. BRANDT (COPENHAGEN). **The Influence of Posture on Kidney Function.**

Posture influences the function of the kidney and the influence is usually attributed to the variation in the pulse pressure found when posture is changed. It is by some held that the variations are not compatible with the filtration-reabsorption theory of renal function. A fact generally overlooked is however that the colloid content of the blood changes with posture. This has been demonstrated by Thompson, Thompson and Dailey and the present study intends to correlate this factor with the function of the kidney.

In a series of experiments the amount of blood cleared of creatinine each minute after ingestion of creatinine was determined. This amount shall as earlier demonstrated, according to the filtration-reabsorption theory be identical with the amount of glomerular filtrate formed each minute.

The glomerular filtrate so estimated changes with change of posture and the change is in each experiment dependent on the variations in the content of proteins of the plasma (refractometrically determined).

The magnitude of the variations may be shown by the following examples from an experiment.

	PROTEIN	AMOUNT OF BLOOD CLEARED OF CREATININE PER MINUTE FILTRATE	AMOUNT OF URINE PER MINUTE
	<i>per cent</i>	<i>cc.</i>	<i>cc.</i>
Standing	8.40	141	0.84
Recumbent	7.98	158	14.49
Standing	8.84	135	1.74

The fact that the creatinine excretion varies with the protein content of the blood is held to indicate that the creatinine is excreted through the glomeruli. From the filtrate formed water is reabsorbed in different amounts under the different circumstances and the variations produced in the solid constituents depend on the ease with which they diffuse back into the blood during the concentration process in the tubules.

REIN, H. (FREIBURG I.B.). **Über die Bedeutung der wichtigsten Gefäßgebiete für Blutdruck- und Wärmeregulation und ihre gegenseitige Abhängigkeit.**

Zu wärmeregulatorischen Zwecken werden vom Organismus des Warmblüters Verschiebungen des Blutes nach der Peripherie oder aber nach den Eingeweiden vorgenommen. Die gleichen Gefäßgebiete müssen aber gleichzeitig auch zur Regulation des Blutdruckes herangezogen werden.

Durch gleichzeitige unblutige Messung der mittleren Durchblutung von jeweils 4 verschiedenen Gefäßgebieten mit Hilfe der "Thermo-Stromuhr" (H. Rein, Zeitschr. f. Biol., LXXXVII, 394, 1928) über lange Zeiten am praktisch wachen Tier liess sich zeigen, dass alle Gefäßgebiete, die im Interesse der Wärmeregulation erweitert sind, nicht zur Druckregulation verengt werden können, während umgekehrt zu wärmeregulatorischen Zwecken verengte Gefässe zur Druckregulation weiter verengt werden können. Ein starker Abkühlung ausgesetztes Tier reguliert seinen Blutdruck deshalb nie mit den Eingeweidegefässen, während ein von aussen geheiztes Tier nur diese zur Druckregulation benutzt. Niere und Gehirn werden normalerweise weder zur Druck- noch zur Wärmeregulation verwendet. Ihre Durchblutung hängt nur vom Gesamtblutdruck ab. Eine besondere Bedeutung kommt der Carotis externa zu. Temperaturreizung der dem N. Ethmoidalis zugehörigen Thermorezeptoren bedingt Durchblutungsänderungen der Carotis externa von ca. 50 Prozent. Eine durch Kühlung der Nase erweiterte Carotis zeigt eine erhebliche Unterempfindlichkeit für Adrenalin. Jede Durchblutungsänderung der Carotis wird aber auch mit Blutdruckregulatorischen Gefässveränderungen in anderen Gebieten (Bauch) beantwortet. Der Trigeminus gewinnt dadurch Einfluss auf die gesamte Druck- und Wärmeregulation des Körpers. Unterbindung einer oder beider Carotiden stellt eine schwere Schädigung des Druck- und Wärmeregulationsvermögens dar.

REIN, H. (FREIBURG I.B.). Die Thermo-Stromuhr. Ein Verfahren, welches mit etwa ± 10 Prozent Genauigkeit die unblutige langdauernde Messung der mittleren Durchflussmengen an gleichzeitig 1-4 Gefässen gestattet. (Demonstration) (Zeitschr. f. Biol., LXXXVII, 394).

REINER, L. (BUDAPEST). Über die Formol-Titrationskurve von Hühnereialbumin bei Gegenwart starker Elektrolyte.

Unter Formoltitrationskurve verstehen wir eine Kurve, die die Formaldehydbindung eines Ampholyts in ihrer Abhängigkeit von dem pH, gemessen durch die gebundene Lauge, bei Gegenwart von überschüssigem Formaldehyd darstellt. Diese Kurve ist, obwohl die ihr unterlegende Reaktion nicht ganz reversibel ist, bis pH 9 eine wohldefinierte; es binden nämlich nur die hydrolysierten NH_2 -Gruppen Formaldehyd und die Hydrolyse ist selbstverständlich reversibel. Einen Beweis hierfür erblicken wir darin, dass beim isoelektrischen Punkt oder unterhalb dessen, das Eiweiss durch Addition von Formaldehyd nicht saurer wird.

Bei einem bestimmten pH ist die Formaldehydbindung erheblich grösser als die Alkalibindung bei Abwesenheit von Formaldehyd und demselben pH. Dies spricht dafür, dass die hydrolysierten -NH_2 mit den ionisierten -NH_3^+ Gruppen in Gleichgewicht sind; dieses wird durch Bildung des Formaldehydkomplexes verschoben.

In neutralisalzhaltigem Medium ist die Formaldehydbindung grösser als in salzfreiem. Das Ausmass dieser Wirkung ist, auf gleiche Grade von Proteinsalzbildung (Ionisation) bezogen, ebenso gross wie die Wirkung, die Neutralsalze auf die Alkalibindung bei Abwesenheit von Formaldehyd ausüben; sie findet aber bei einem viel geringeren pH statt.

Bei pH 9 werden die Messungen weniger gut reproduzierbar. Es erfolgt hier eine Denaturierung des Proteins, die der "Alkalidenaturierung"

entspricht und auch bei derselben Ionisation erfolgt. Der Versuch zeigt aber, dass die Denaturierung nicht von der Alkalinität, sondern vom Grad der Ionisation abhängt. Dies lässt vermuten, dass gewisse Bausteine des Eiweisskomplexes durch ausserordentlich lockere, elektrostatische, doppelsalzartige Bindungen zusammengehalten werden. Diese werden durch starke einseitige Ionisation gespalten.

REINER, L. (BUDAPEST). **Electrodialysis Apparatus. (Demonstration)**

RICHET, CHARLES, FILS (PARIS). **La mort aux fortes dépressions barométriques.**

Les animaux soumis aux fortes dépressions barométriques présentent une série de troubles physiologiques aboutissant à la mort. D'après nos recherches, effectuées presque toutes avec Behague et Garsaux, elle survient dans trois circonstances différentes:

1. Au cours d'une dépression barométrique poussée très loin, l'animal restant au repos.

2. Au cours d'une dépression barométrique poussée moins loin, l'animal effectuant un dur travail c'est la *mort par fatigue*.

3. Quelques heures après une dépression barométrique poussée très loin, l'animal étant revenu au sol et à ce moment paraissant normal; c'est la *mort tardive*.

1. Peu de choses sont à dire, depuis les travaux de Paul Bert, Mosso, Haldane et Barcroft, sur la mort au cours d'une dépression barométrique poussée très loin.

A notre avis, ce ne sont ni l'asténie, ni les crises convulsives, ni le coma, qui indiquent l'imminence de la mort, ce sont les phénomènes respiratoires, qui se déroulent en trois phases successives: la polypnée, l'oligopnée, puis l'anisopnée. Cette anisopnée exige, sous peine de mort, la descente rapide, ou l'arrivée d'oxygène en excès.

L'altitude maximale peut-elle être modifiée par certaines conditions extra-physiologiques?

Nous avons diminué la susceptibilité du système nerveux par l'injection de morphine (1 cg. par kg. chez le lapin). Il n'y a pas de différence. Nous avons ensuite diminué le champ de l'hématose en pratiquant chez le cobaye un pneumo-thorax unilatéral. Cet animal supporte aussi bien la dépression qu'un animal normal.

La saignée (25 à 45% du sang des cobayes ou des lapins) ne modifie pas de façon appréciable l'altitude qu'atteint l'animal. Même combinée au pneumo-thorax la saignée n'a pas d'influence.

Refroidi artificiellement par immersion dans l'eau froide l'animal (lapin ou cobaye) résiste davantage que l'animal normal et ce fait est tout à fait comparable à la résistance plus considérable à l'asphyxie ordinaire des animaux refroidis.

Les ascensions antérieures modifient légèrement la sensibilité de l'animal.

2. *Mort au cours d'une dépression moins fortement poussée chez un animal qui travaille*.—Au cours de recherches sur le travail aux altitudes nous avons observé l'apparition de morts brutales à des altitudes relativement basses.

Nous forçons le lapin à marcher dans un tambour qui tournait avec une certaine rapidité.

Sur une vingtaine d'expériences nous avons eu deux morts subites.

Le lapin 230 monte à 12.500 mètres dans une atmosphère très riche en oxygène. Il supporte parfaitement cette altitude.

Tout en continuant à maintenir le débit d'oxygène au maximum, on fait alors tourner le tambour et l'animal, pendant deux minutes 30 secondes, fait de vigoureux efforts, puis il tombe; il est mort. Or, dans les conditions habituelles d'oxygénation où nous nous étions mis, le lapin résiste au moins jusqu'à 15.000 mètres. C'est donc bien de fatigue à l'altitude qu'il est mort.

Dans l'expérience 215 nous avons fait monter un lapin jusqu'à 9.000 mètres, altitude que, au repos, il supporte parfaitement.

Sur le palier de 9.000 m. l'animal, après avoir effectué un travail énergétique durant 30 secondes, tombe mort.

Cette mort par fatigue, à notre connaissance, n'a pas encore été décrite.

3. Dans quatre cas sur plusieurs centaines d'expériences, nous avons observé la mort tardive.

Les animaux sortis du caisson à dépression avaient repris leur apparence habituelle sans crises convulsives ni asténie considérable. Mais dans la nuit ou le lendemain, ils succombèrent. Nous n'avons pu déceler la cause de cette mort tardive. Nous la considérons comme comparable à la mort tardive que nous avons observée dans des expériences déjà anciennes, chez le chien ayant respiré en vase clos durant plusieurs heures.

RICHTER, C. P. and M. E. BRAILEY (BALTIMORE). **On the Regulation of the Normal Water-Intake in Rats and Its Experimental Modification Through Brain Punctures (Experimental Diabetes Insipidus).**

Daily water-intake was measured in 52 rats, 25 females and 27 males from 30 to 160 days of age. It increased gradually with age, and was greater in the males than in the females (at 30 days 16 cc. for the females and 19 cc. for the males, and at 160 days 25 cc. for the females and 34 cc. for the males). The gradual increase in water-intake with growth in the female as well as in the male suggested its relationship to body-weight. But body-weight was found to increase very much more rapidly than water-intake. There was, however, a perfect correlation with body-surface. At ages from 30 to 160 days all rats of either sex drank about 800 cc. per square meter body-surface per day. Calculated for man on the same basis the water-intake would be 1500 cc., which is very close to what is generally considered to be the normal average. It may be that this principle has general applicability to all mammals.

Various attempts have been made to modify water-intake, but we will report only our results produced by punctures made in the brain stem. Lesions were made through the base of the brain with a fine scalpel in the region of the sella turcica. In 13 out of 40 animals increase in water-intake was produced. In one animal the water-intake increased from 25 cc. to 260 cc. per day, the maximum intake representing twice the animal's own body-weight. In others the increase was not so marked. The diabetic state seemed permanent, for at the time the animals were killed the water-intake was still as high as at the beginning six months before. Histological studies of the brain are being made.

RIDDLE, OSCAR (COLD SPRING HARBOR, N. Y.). Thyroid Size in the Sexes.

Weights were obtained on the thyroids of 1917 healthy ring doves and on 602 healthy common pigeons aged 4-36 months. Within these age limits there is little or no change in body weight, and in many of the 71 races or strains studied there is little or no change in thyroid weight. The large influence of the hereditary factor in thyroid size, and many well-known physiological factors, have here been adequately equalized or controlled; but thyroid weight nevertheless shows itself to be highly variable. Mean values obtained from the union of all (71) comparable races of ring doves indicate an excess weight (per unit body weight) in the females of 4.5 per cent, or of 1.8 per cent. This mean for 19 races of common pigeons is 7.0 per cent. In general, those races which have the *smallest* thyroids show the *smallest percentage sex difference in thyroid size*; in races characterized by *larger* thyroids, the *female glands exceed those of the males by a notably higher percentage*. We interpret these facts as indicating that many individuals of these races have thyroid enlargements similar to those of endemic goitre; and that, as in the human, the females are more often thus affected than are the males.

The rather current impression that the normal thyroids of human females are larger than those of males is probably supported only or mainly by data from races or regions in which thyroid size tends to be high in both sexes—but specially high in the females—because of slight or pronounced tendencies and approximations to endemic goitre; and also because of temporary enlargements of the female thyroid at certain phases of reproduction.

A true sex difference in normal thyroid size has not yet been demonstrated in any species. The definite fact that endemic goitre shows a higher incidence in human females than in males, and the probabilities here indicated that the same is true in doves and pigeons, provide some evidence that this aspect or degree of hypothyroidism is more frequently observed in the females of all of the three species hitherto satisfactorily examined.

RIJLANT, PIERRE (BRUXELLES). Contribution à l'étude des centres d'automatisme du coeur du mammifère.

Dans le coeur du mammifère le battement naît au niveau du noeud de Keith-Flack (sinus). Ce territoire sinusal est le siège d'une contraction qui précède de 10 à 15 σ celle de l'oreillette droite (Rijlant, 1923; Athanasiu, 1925).

L'activité du territoire sinusal est précédée d'une contraction naissant dans la veine cave supérieure (Rijlant). Cette contraction représente l'activité initiale du coeur du mammifère.

Par les méthodes myographiques et les méthodes électrographiques classiques on n'est pas parvenu jusqu'ici à dissocier nettement les lieux d'origine de ces activités du coeur. C'est pourquoi nous avons adapté aux nécessités de l'électrophysiologie cardiaque, les méthodes d'oscillographie cathodique introduites en physiologie par Gasser et Erlanger.

Nous avons étudié l'activité automatique normale du coeur in situ (chat, chien, lapin) celle du coeur excité par le pneumogastrique ou le sympathique ou soumis à l'action de l'acétylcholine ou de l'adrénaline.

Nous avons étudié aussi le coeur isolé, l'oreillette droite isolée, les

régions sinusale et veineuse isolées, maintenues à l'état physiologique ou réagissant à l'excitation de leurs nerfs vague ou sympathique ou soumises à l'action de l'acétylcholine et de l'adrénaline.

I. Coeur in situ normal. Les courbes oscillographiques obtenues aux dépens de la région sinusale montrent une onde sinusale qui précède l'activité auriculaire proprement dite de 3 à 7 σ . Cette onde qui atteint sa plus grande amplitude en 1 à 2 σ , présente les mêmes caractéristiques d'accélération que l'onde auriculaire. Son amplitude diminue en général avant le début de l'onde auriculaire. Cette onde n'existe pas dans les courbes obtenues dans les dérivations n'intéressant pas le territoire sinusal.

L'exploration de la région terminale de la veine cave démontre que l'activité sinusale est précédée d'une activité à développement lent. L'intervalle existant entre les activités veineuse et sinusale est de 5 à 10 σ .

Le bloc partiel ou total a été obtenu par l'excitation du pneumogastrique, l'acétylcholine ou par des incisions entre les différents territoires.

II. Tissus isolés. Les expériences sur les tissus isolés nous ont donné les mêmes résultats et nous ont permis d'isoler les différentes activités.

ROAF, H. E. (LONDON). **Discrimination of Colour.**

In the retinae of amphibia, reptiles and birds there are coloured globules situated at the junction of the inner and outer limbs of the cones. In view of the fact that colour vision can be explained by colour filters in front of certain of the percipient elements¹ a spectroscopic examination has been made of the globules from the retinae of hens. Red, yellow and almost colourless faint green globules are present. The photographs of the spectra show that the red globules absorb light from the violet end up to about 5900 Å whilst the yellow ones absorb up to about 5000 Å. These values are close to the regions of maximum discrimination by the human eye.

If colour vision in man depends upon two different kinds of colour screens and a third group of unscreened receptors, it is possible that the unscreened receptors may be the rods. In this case stimulation of the rods would be associated with a sensation of blue² and it is probable that recognition of detail will be less with the shorter wave-lengths corresponding to blue light than with the longer ones. Experiments indicate that this is the case.

ROBB, JANE SANDS (PHILADELPHIA). **The Elemental Character of Embryonic Electrocardiograms.**

Action currents obtained from 24 to 36 hour chick embryo hearts yielded waves which were monophasic. Associated with the differentiation of heart chambers, the electrocardiogram became more complex. A typical P-Q-R-S-T series, comparable to that in the adult human, appears between 50 and 72 hours.

To test the authenticity of these "slack string" monophasic records the use of a resistance coupled amplifier has been necessary. The significance of these observations will be discussed with reference to the diagnosis of human cardiac pathology.

¹ H. E. Roaf. *Quart. Journ. Exper. Physiol.*, 1927, xviii, 243.

² W. O. Siven. *Skand. Arch. f. Physiol.*, 1905, xvii, 306.

ROCHE, ANDRÉE (STRASBOURG). **Le problème de l'assimilation des pentosanes peut-il être ramené à celui de l'assimilation des pentoses?**

Les travaux de Stone et Jones, de Weiske et Slowzoff, ont établi que 50% environ des pentosanes ingérés peuvent être retenus par certains animaux. Cette assimilation est-elle due à une transformation digestive des pentosanes en pentoses ou à une fermentation intestinale productrice d'acides gras, comme c'est le cas pour la cellulose? Pour élucider ce problème, nous avons dû préalablement établir une méthode de dosage des pentoses dans le sang, basée sur la non fermentescibilité de ces sucres. Un pentose ajouté à du sang in vitro est retrouvé quantitativement dans le reste de fermentation et peut donc être dosé par réduction. Le reste de fermentation du sang étant sensiblement constant chez un animal donné, une augmentation de ce reste, consécutive à une ingestion de pentoses devra être rapportée à ceux-ci. Dans une série d'expériences faites sur le lapin et sur la chèvre, nous avons observé qu'après ingestion d'arabinose ou de xylose (de 0,5 à 2 gr. par kg.), le reste de fermentation du sang augmente de 300 à 500%. Après ingestion de pentosanes (10 gr. par kg.), le reste de fermentation du sang demeure au contraire remarquablement constant. Ce résultat peut s'expliquer soit par une transformation lente des pentosanes en pentoses et une absorption très lente de ces derniers, soit par le dégradation intestinale des pentosanes—et éventuellement d'une petite quantité de pentoses formés—en acides gras. Les travaux de Salkowski et Slowzoff viennent à l'appui de cette dernière hypothèse.

Il semble donc que, contrairement à l'opinion de Magnus-Levy, le problème alimentaire des pentoses ne puisse se ramener à celui des pentosanes. L'ingestion de ceux-ci, comme celle de la cellulose, doit réaliser, grâce aux fermentations intestinales, un apport, non pas en hydrates de carbone, mais en acides gras.

ROCHE, JEAN (STRASBOURG). **Recherches sur la globine.**

Cette communication expose les résultats de recherches: (1) sur la combinaison de la globine naturelle avec l'hématine alcaline (Hill et Holden); (2) sur les propriétés physico-chimiques de la globine naturelle ou dénaturée (point isoélectrique et courbes de neutralisation); (3) sur les modifications du point isoélectrique et des propriétés (courbes de neutralisation et de solubilité) de la globine au cours de sa dénaturation et de l'action sur elle des acides et des bases.

ROGOFF, J. M. and G. N. STEWART (CLEVELAND). **Functions of the Adrenal Glands.**

It has been well established that the function of the epinephrin secretion from the adrenals is not indispensable. The important function of the glands consists of the elaboration and probably secretion of a hormone by the cortex. To distinguish this hormone from adrenalin and to indicate its origin in the interrenal tissue, we have employed the name, "Interrenalin." Marked prolongation of life has been observed by us in adrenalectomized animals when extracts of adrenal cortex were administered. Beneficial influence has been obtained, in a number of cases of Addison's disease, by administration of these cortical extracts.

RONDONI, PIETRO (MILANO). **L'influenza di una dieta a base di timo sul ratto, con particolare riguardo alla reattività infiammatoria.**

Ho voluto studiare gli effetti che sull'organismo del ratto adulto può

esercitare la prolungata somministrazione di una dieta costituita esclusivamente o largamente da *timo di vitello*, nell'intento di stabilire, oltre ad eventuali modificazioni corporee generali, se esistano modificazioni della emopoiesi, come sono state constatate per effetto della dieta con fegato ed anche con rene; di studiare il ricambio purinico in rapporto all'elevata somministrazione di nucleoproteidi; e di stabilire soprattutto *se in conseguenza di una dieta iperproteinica ed iperpurinica è modificata qualitativamente e quantitativamente la risposta agli stimoli infiammatori di varia natura*. Si mantennero per parecchie settimane i ratti ad una dieta costituita da timo solo oppure da timo mescolato con pane o con farina di mais.

Si notò sempre una netta diminuzione di peso negli animali, più spiccata-mente per effetto della dieta timica esclusiva. Si osservò spesso una modica diminuzione del numero delle emazie circolanti, qualche volta presenza di emazie nucleate in numero di poco superiore allo scarso reperto normale. I leucociti (la cui cifra normale fu di regola bassa nei miei ratti, inferiore a quella data come media nella nota monografia di Klieneberger) offrono un aumento modico: così in una serie sperimentale da 7.000-9.000 per mmc. a 17.000-18.000. Aumentano proporzionalmente i linfociti grandi in confronto ai piccoli; ed i mononucleati e forme di passaggio. Nel midollo osseo (strisci colorati secondo May-Grünwald-Giemsa) sembrano proporzionalmente aumentare le forme riferibili ad attività leucoblastica.

Si suole trovare un aumento del peso relativo del fegato e soprattutto del rene in confronto a ratti normali coetanei e di eguali dimensioni. L'aumento del peso percentuale (rispetto al peso corporeo) del rene si verifica anche se si rapporta il peso dell'organo al peso iniziale più elevato dell'animale; ed è per ciò non apparente, ma reale, in dipendenza dell'esaltata funzione dell'organo nella smaltire maggior quantità di cataboliti azotati e forse anche di fenomeni degenerativi.

La milza non offre modificazioni apprezzabili di peso.

La colorazione vitale col trypanblau ha messo in evidenza una maggiore colorabilità diffusa negli animali a dieta timica in confronto ai controlli a dieta normale iniettati con quantità di colore proporzionali al peso.

La iniezione sottocutanea di istamina, peptone, olio di trementina, soluzione di urato monosodico-acido urico (in proporzioni tali da risultare un pH = 7,2 circa) ha dimostrato che i ratti a dieta timica posseggono spesso una certa ipersensibilità agli stimoli flogogeni: fenomeni iperemici più spiccati e durevoli, con tendenza alla emoragia; più abbondanti fenomeni essudativi; e, in uno stadio avanzato, fenomeni proliferativi più intensi. Si hanno naturalmente molte differenze individuali nella risposta allo stimolo; ma risulta frequente una specie di *allergia aspecifica* nell'animale a dieta di timo, specialmente di fronte al peptone ed alla soluzione di urato-acido urico. Questa ultima constatazione può avere importanza per la spiegazione dei sintomi infiammatori nella gotta.

L'esame istologico in corso pare dimostrare lesioni degenerative in vari organi; e soprattutto i segni di una modificazione funzionale della tiroide.

Lo studio del metabolismo dell'azoto è pure in corso.

Si cerca anche di stabilire se esistono modificazioni del pH dei tessuti, mediante il metodo di Rous della iniezione intravitale di indicatori della serie delle ftaleine.

RONZONI, ETHEL and MICHAEL SOMOGYI (ST. LOUIS). **The Mechanism of Fermentation of Glucose, Sucrose and Maltose by Yeast.**

The differences in the mechanism of fermentation of glucose, sucrose and maltose have been investigated using gasometric and chemical methods. Curves of the rate of fermentation and chemical determinations of the nature of the sugar present at different stages indicate the following facts.

1. The rate of fermentation of glucose and sucrose are identical.
2. Within wide limits the CO_2 production is independent of the concentration.
3. If the absolute amounts of either glucose or sucrose and of yeast are kept constant, the rate of fermentation is constant, with dilutions up to four times the original volume of the mixture. These facts indicate that diffusion is not involved in this process, and that therefore fermentation must take place at the cell surface. The disappearance of these sugars from solution before the production of CO_2 is complete suggests adsorption by the yeast cells.
4. The hydrolysis of sucrose takes place so rapidly that it is not the factor which limits fermentation of the resultant simple sugars. Shortly after fermentation has started (three to five minutes) the unfermented fraction of sucrose added is present as invert sugar. Invertase is present in the water in which yeast has been suspended, even though changed daily for a period of a month. Zymase and maltase are not.
5. Maltose is fermented much more slowly than glucose and sucrose, and the rate is increased with increase of concentration.
6. When the absolute amount of maltose and yeast are constant, dilution causes a decrease in the rate of fermentation.
7. All of the reducing substance in the liquid phase is present as unchanged maltose. This indicates that maltose is split within the cell, and that the rate of fermentation depends on the rate of diffusion. Since the rate is not doubled by doubling the concentration of maltose, some other factor must also be involved. This factor cannot be the removal of the glucose formed, since a much faster rate is shown for glucose itself. It must therefore be the action of maltose within the cell.

ROOS, J. (UTRECHT). **Action Currents from Smooth Muscle.**

Records have been made of the action currents from the intestine of the cat and of the rat, by leading off the current in different ways and under different conditions.

We were able to get electrograms of peculiar form and of striking regularity, and we came to an explanation of the form of the action current lead off by placing one electrode on an injured, and the other on an uninjured part of the intestine.

ROQUE, FRANCISCO T. (SAN FERNANDO, P. I.) and ARNO B. LUCKHARDT (CHICAGO). **Effect of Stimulation of the Central End of Motor Branches of the Femoral Nerve on the Knee Jerk.**

Using the Johnson¹ knee jerk apparatus for eliciting and registering the knee jerk in the dog, it was found that stimulation with a faradic current of the central end of the contralateral nerve to the quadriceps extensor

¹ C. A. Johnson. Amer. Journ. Physiol., 1927, lxxxii, 75.

muscle usually caused an exaggeration of the knee jerk but sometimes an inhibition. Stimulation of the central end of a branch of the femoral nerve motor to the quadriceps of the ipsilateral side produced opposite effects depending on the time of stimulation. If the nerve was stimulated briefly just prior to the tap on the ligamentum patellae, an exaggeration of the knee jerk occurred. If the stimulation occurred during the stroke of the hammer on the patellar ligament, there ensued a complete inhibition. Both results could be obtained in some preparations by simple traction on the nerve at the appropriate time. Following transection of the spinal cord in the upper lumbar region, stimulation of the central ends of the muscular branches of the femoral nerve supplying the quadriceps extensor caused solely inhibition. The experiments are interpreted, in part, as showing that the excitability of the knee jerk center can be influenced by impulses coming to it from the effector organ itself. The results, furthermore, would seem to indicate that the exaggeration of the knee jerk involved in some way parts of the nervous system cephalad to the spinal cord transection.

ROSENBERG, H. (BERLIN). Das Verhalten der Negativitätswelle des Nerven bei Ueberschuss von Kalium- und Calciumionen.

Der auch am Nerven beobachtete Antagonismus von K^+ und Ca^{++} gestattete die Annahme, dass die Beziehungen zwischen dem Verlauf des Anstiegs und der Geschwindigkeit der Negativitätswelle im Nerven zu prüfen sind, wenn die zeitlichen Verhältnisse durch beide Ionenarten gegensinnig geändert werden. In den Versuchen, die mit Verstärker und Schleifenoszillograph ausgeführt wurden, zeigte sich aber, dass bei den bisher gewählten Konzentrationen sowohl von K^+ , wie von Ca^{++} stets eine Abnahme der Leitungsgeschwindigkeit eintritt. Auch die Grösse der Aktionsnegativität wird immer vermindert. Bei Ca^{++} -Ueberschuss ist die Anstiegsdauer zwar häufig verkürzt, aber weniger, als der Höhenabnahme entspricht—daher ist die Anstiegsgeschwindigkeit herabgesetzt. Bei K^+ -Ueberschuss wächst die Anstiegsdauer gewöhnlich, und infolge der gleichzeitigen raschen Verkleinerung der Aktionsnegativität sinkt die Anstiegsgeschwindigkeit bedeutend. Die Kaliumversuche bieten gleichsam das Bild fortgeschrittener Calciumvergiftung. Da die Kaliumwirkungen schneller einsetzen und durch Auswaschen vollkommener zu beheben sind als entsprechende Calciumwirkungen, kann man die Unterschiede auf einen rascheren Austausch des Kaliumions zurückführen. Auswaschen nach schwacher Calciumeinwirkung bedingt Veränderungen, die vielleicht auf eine übernormale Beschleunigung des Erregungsablaufs schliessen lassen.

Im Gegensatz zu der Annahme Lillies war in allen Versuchen das Produkt aus der Anstiegsdauer und der Leitungsgeschwindigkeit keine Konstante. Aber zwischen Anstiegs- und Leitungsgeschwindigkeit besteht ebenfalls keine lineare Abhängigkeit. Man muss daher auch die sonstigen Veränderungen im Verhalten des Nerven—z.B. die erhöhte Coulombempfindlichkeit des Kaliumnerven, die verminderte des Calciumnerven—berücksichtigen, wenn man die Zusammenhänge deuten will.

ROSENTHAL, SANFORD M. (WASHINGTON). Studies of Starch Digestion in Normal and Diabetic Subjects.

As a result of studies upon dogs and rabbits, it was found that the rate

of digestion of raw starch, as measured by the increase in blood sugar, is markedly inhibited by acids. One cubic centimeter of 3.6 per cent hydrochloric acid per kilo of body weight will almost completely prevent the intestinal digestion of raw starch for one to three hours. This amount of acid does not affect the rise in blood sugar following glucose feeding.

In humans similar findings were obtained with cooked starches. Cooked starches in man caused a rise in blood sugar as marked as though glucose were given (56 mgm. per cent in one-half hour), but in 9 normal adults 50 to 75 grams of raw starch caused no change in blood sugar. This principle was applied to diabetics and the starch was fed as such, or as raw carrots, turnips, or nuts. In 12 diabetics the raw starch meal produced the following effects on blood sugar (average): In one-half hour an increase of 6 mgm.; in one hour a decrease of 9 mgm.; in two and one-half hours a decrease of 14 mgm. per cent.

ROTHLIN, E. (BASEL). **Über den Wirkungsmechanismus der herzwirksamen Glykoside.**

1. *Beziehungen zwischen Calcium und der Glykosidwirkung.* Calcium-Ionen sind seit Ringer als unbedingt notwendiger Faktor für die normale Herztätigkeit: Erregbarkeit, Reizleitung, Kontraktilität und Tonuslage, erkannt. Die Wirksamkeit der Herzglykoside (Digitoxin-Strophanthin-Scillaren) erweist sich abhängig vom Calciumgehalt. Testobjekt: isol. Froschherz nach Straub.

a) *Nährlösung mit normalem Ca-Gehalt.* Nur ein geringer Prozentsatz der Herzen lässt eine sog. therapeutische Wirkungsphase der Glykoside erkennen, es sind vor allem schwache oder geschädigte Herzen. Normale Herzen lassen nur toxische Erscheinungen erkennen: Arrhythmie, Verkürzungsrückstand und tonischer Stillstand.

b) *Nährlösung mit zu geringem Ca-Gehalt.* Herztätigkeit meist hypodynam; die therapeutische Phase der Glykosidwirkung ist regelmässiger ausgeprägt. Toxische Dosen führen zu den bekannten Vergiftungsercheinungen, tonischer Stillstand weniger ausgeprägt.

c) *Nährlösung ohne Ca-Gehalt:* Herzstillstand, Glykoside regen keine Herztätigkeit an. Die Giftfixation findet aber statt, dies ist nachweisbar durch Zufuhr Ca-haltiger Nährlösung, worauf erst der bekannte Vergiftungsablauf eintritt. Die typische Glykosidwirkung erweist sich abhängig von Ca-Gegenwart und ist für Digitoxin, Strophanthin und Scillaren gleichsinnig. Ohne Calcium keine tonische Kontraktur (Loewi).

2. *Reversibilität der Glykosidwirkung.* Die Haftfestigkeit ist eine der charakteristischen und therapeutischwertvollen Eigenschaften aller typischen Herzglykoside. Am isol. Herzen nach Straub wurde sie durch Auswaschversuche geprüft. Die Untersuchungen mit Digitoxin Merck und Cloetta, sowie Digitaline Nativele ergeben, dass die Auffassung von De Giacomi und Fischer, reines Digitoxin Cloetta führe in 100 Prozent der Fälle zu irreversiblen tonischen Ventrikelstillstand, nicht richtig ist. Denn die Wirkung (Ventrikelstillstand) aller 3 Digitoxine ist entsprechend ihrer analogen Giftigkeit am Frosch (zeitlose Methode) bis zu einer bestimmten Grenzkonzentration, 1:150,000–200,000 für 1 ccm und 1:100,000 für $\frac{1}{2}$ ccm. Kanüleninhalt, gleich gut reversibel, vorausgesetzt, dass der Auswaschversuch lange genug durchgeführt wird. Die Herztätigkeit nach vollständigem Herzstillstand kann durch Auswaschen die normalen Werte von Frequenz und Hubhöhe erreichen. Im Vergleich

zum Scillaren weist Digitoxin eine geringere Auswaschbreite auf, d.h. der Bereich der zum Stillstand führenden und auswaschbaren Scillaren-Konzentrationen ist grösser als jener für Digitoxin. Starke Scillaren-Konzentrationen sind ebenso wenig auswaschbar wie jene von Digitoxin.

ROWE, ALLAN WINTER and MARY McMANUS (BOSTON). **Metabolism of Galactose. VIII. Non-Diabetic Glycosurias.**

In a series of over three thousand cases correlation studies have been made between the tolerance for galactose, blood sugar levels, and the appearance of a spontaneous glycosuria. The relationship of blood sugar levels and glycosuria in diabetes is contrasted with the same observations in large groups presenting several endocrine and non-endocrine disorders. Analysis of these demonstrates the complexity of the mechanism regulating carbohydrate metabolism and the complete independence of many spontaneous glycosurias from blood sugar levels. Pituitary, thyroid, and ovarian cases presenting certain aberrant functions show glycosuria with normal or low normal sugar levels, while in disease of the adrenals (Addison's) a glycosuria is frequently observed with blood sugar levels even below a low normal. Of the non-endocrine factors various injuries to the central nervous system, hepatic disorders, syphilis, primary anaemia, and the leukaemias all show a fairly frequent incidence of glycosuria with only exceptionally a blood sugar level above the conventional normal. The anomalous carbohydrate metabolism during pregnancy is also considered, and the existence of a renal glycosuria discussed.

ROWNTREE, LEONARD G. and ALFRED W. ADSON (ROCHESTER, MINNESOTA). **The Effects of Sympathetic Ganglionectomy and Ramisectomy in Arthritis.**

The clinical findings in an advanced case of arthritis deformans in a young woman of thirty-six suggested the possibility of a relationship between excessive vasoconstriction and the arthritic symptoms. The coldness of the extremities was extreme, with marked sweating, tender, painful and swollen joints and trophic changes in the muscles, skin and nails. In June, 1926, the second, third and fourth lumbar sympathetic ganglia on both sides were removed with immediate and complete cure of the arthritis in the lower extremities which has persisted for three years.

Following this operation the patient had no symptoms of arthritis below the waist but was the victim of crippling and disabling arthritis in the upper extremities. The results of the first operation were so gratifying that when the possibility of a second operation to relieve the upper extremities was suggested, she returned with great joy. The removal of the first and second dorsal ganglia and the cervico-dorsal ganglia on both sides in November, 1928, has resulted in almost complete disappearance of the arthritis in both upper extremities. The hands are now warm and dry and there has been complete relief from pain in both hands with only the mildest kind of residual manifestations of arthritis in the wrists, right elbow and right shoulder.

These results indicate that the nervous system is playing a much greater rôle in the phenomena of arthritis than has hitherto been supposed. The lapse of further time and the results in additional cases are necessary before a final evaluation of the effects of sympathectomy in this form of arthritis can be determined. However, sympathetic release has been effected in

five additional cases with results which appear very promising. The distal joints of the extremities are earliest and most favorably affected and the periarticular lesions yield more readily than the osseous lesions.

SAIKI, A. K. and G. A. TALBERT (GRAND FORKS, NORTH DAKOTA). **Uric Acid in the Sweat, also in the Blood and Urine as Affected by Sweating.**

The uric acid content was determined in the sweat, also in the urine and blood before and after sweating. Methods of Folin, Benedict and Brown were employed alternately. The method of Benedict gave a little higher reading than the other two.

Of the 44 experiments on 17 different subjects all showed the constant presence of uric acid in sweat ranging from a minimum of 0.77 to a maximum of 2.52 mgm. per 1000 cc. Sweating increased the uric acid content of the blood and urine in 90 per cent and 82 per cent of cases respectively. However, no definite correlation is indicated of the sweat content to that of the blood and urine.

SALANT, WILLIAM (COLD SPRING HARBOR, NEW YORK). **Pharmacological and Physiological Studies on the Autonomic Nervous System.**

Salts of mercury injected intravenously into anaesthetized cats increase the irritability of the parasympathetic system, cardiac inhibition steadily increasing with successive injections of doses of one or two milligrams per kilo. But the effect usually reaches a maximum after several doses are given when the peripheral endings of the cardiac vagus no longer react to the interrupted current of the same strength to which they responded before. The stimulation produced by mercury was also observed in experiments with atropine, much larger doses being necessary to paralyze the vagi when mercury is given. It was also observed that mercury stimulates the parasympathetics in the intestines. Intestinal motility was greatly increased after amounts of 3 to 4 mgm. of mercury per kilo were injected in divided doses, but the effect subsided after the administration of much larger doses. The sensitization of the vagal terminations by small doses of pilocarpine greatly increased the effect of mercury. But this action of mercury was not observed when atropine was given before. The rhythmic contractions were, on the contrary, depressed by mercury. Evidence was also obtained showing that the inhibitory fibers of the vagus are also stimulated by this substance.

Stimulation by the interrupted current was much more effective after than before mercury as a subminimal current produced very powerful contractions. Functional variation in the vagus mechanism as well as in the cardiac accelerators may modify the action of mercury on the heart. Increased irritability of the one lowers the tolerance, while the same change in the other renders the heart more resistant to mercury. This was demonstrated by means of pilocarpine and by stimulation with the interrupted current for the vagus, and with the aid of adrenalin for the sympathetic. The effects of mercury were greatly increased when it was given after ergotamine. Mercury was even more toxic after complete denervation of the heart.

SALIT, P. W. and H. A. MATTILL (IOWA CITY). **Biochemical Studies of the Ocular Humors and the Lens with Special Reference to Cataract.**

This study on normal eyes and human senile cataracts was undertaken

with the supposition that the physiological condition of the lens is dependent to a great extent upon the chemical nature of the humors surrounding it.

The sodium chloride content of the humors of beef eyes is slightly less than that of the blood plasma, 714 mgm. per cent for the aqueous, 682 mgm. per cent for the vitreous. The lens contains only about one-half that amount. Reducing sugar occurs in different amounts in the two humors and the lens, and decreases with advancing age. The following are the figures in milligrams per cent for 5-week-old calves and 2-year-old cattle: Lens 144.8, 135; vitreous 58.1, 54.1; aqueous 108.0, 86.4. In its calcium content, the aqueous resembles very closely the spinal fluid, 5.0 mgm. per cent. The vitreous contains 7.2 per cent of calcium. No calcium could be demonstrated in normal animal lenses nor in five human lenses in the early stages of cataract. Analyses of 46 lenses from older cataracts revealed enormous amounts of calcium, varying from 2.8 mgm. per cent to 104 mgm. per cent. The average cholesterol content of normal beef lenses is 44 mgm. per cent. That of the normal human lens is identical with that of the upper limit of the plasma, 0.18 per cent. The cholesterol values of human senile cataracts vary from 0.19 per cent to 0.89 per cent. The range of the lecithin values of the same cataract lenses is 0.48 to 1.88 per cent. For normal beef lenses the average lecithin content is only 111 mgm. per cent. Both the weight and the nitrogen content of normal beef lenses increase practically at the same rate during the first two years of growth with a corresponding decrease of the water content. The H ion concentration of both humors appears to decrease with age as do the CO₂ content and capacity.

These changes and particularly the marked increase in calcium as well as cholesterol and lecithin in cataract lenses lend support to the idea that denaturation of the lens protein is the explanation of cataract formation.

SAMOJLOFF, A. und M. KISSELEFF (KASAN). Der Verlauf der Reflexe an der dekapitierten Katze in Abhängigkeit von der Lage der Extremitäten.

Die Grösse des reflektorischen Effektes an einem Beine ist eine Funktion des Zustandes des anderen symmetrischen Beines. Erzeugt man an der einen unteren Extremität einen rhythmisch sich wiederholenden Flexorenreflex und verändert dabei die Beugung des Knies an der symmetrischen Extremität, so sieht man, wie der Flexorenreflex die Werte von Null bis zu maximaler Grösse annimmt. Der Flexorenreflex kombiniert sich in diesem Falle mit dem Philippson'schen Reflexe.—Eine ähnliche Beziehung besteht auch zwischen dem Kniesehenreflexe der einen Extremität und dem Dehnungsgrade des Quadriceps der anderen Extremität.—Der Grad der Vollkommenheit der Plastizität soweit dieselbe sich in der Verlängerungs- und Verkürzungsreaktion äussert, gehört ebenfalls in die Gruppe der in Rede stehenden Erscheinungen. Nach Wunsch ist es möglich, an einem und demselben Praeparat eine bessere oder schlechtere Plastizität des einen Beines zu erzeugen, wenn man nur den Dehnungsgrad des Quadriceps des anderen Beines berücksichtigt.—Die Dehnung des Quadriceps (sämtliche Muskeln der unteren Extremität unbeweglich gemacht) bietet einen bestimmten Widerstand; letzterer ist in hohem Grade abhängig vom Zustande des Quadriceps der anderen Seite. Der

Dehnungsgrad des einen Muskels ist verantwortlich für den Ablauf der Reflexe in einem anderen Muskel.

SATAKE, Y. and T. KOJIMA (SENDAI). Suprarenal Insufficiency in Rabbits.

With 77 male rabbits, the main suprarenal glands were extirpated by a two-stage operation with an interval of 11 to 340 days. One-seventh died within 7 to 11 days after the last operation. The others were able to survive much longer; one-fifth of the total survived over one year and one-fifth over 500 days. In 3 rabbits which died within 7 to 10 days no accessory cortical tissue could be detected. In those which survived longer, accessory tissues were invariably found, and there was shown to exist a somewhat close relation between the duration of survival and the amount of the accessory cortical tissues hypertrophied.

Next the total extirpation of the accessory cortical tissues besides both the main suprarenals was performed in rabbits by a 4-stage operation. In the majority of cases this was successfully done. The longest survival duration of those cases deprived of all the cortical tissues was recorded as 5 weeks; seventy per cent died within 14 days. Outstanding anatomical changes in the rabbits which died on the total removal of the cortical tissue were congestion and hemorrhage in the intestinal tract, though the severity differed from case to case and in a few cases they were absent.

SBARSKY, B. I. (MOSKAU). Aminosäuretherapie.

Der Verfasser, sich auf seine früheren Arbeiten über "Adsorption von Aminosäuren durch die Formelemente des Blutes," fussend, hält es für möglich eine Arbeitshypothese über die Verwendung einiger Aminosäuren als therapeutisches Mittel bei Infektionskrankheiten aufzustellen.

Die Grundlage der Hypothese besteht darin, dass bei der Injektion von Aminosäuren eine übergehende Erhöhung der Konzentration derselben im Blute erfolgt. Die Zellen verschiedener Organe besitzen die Eigenschaft einige Aminosäuren in grösserer Menge zu absorbieren als andere. Dieser Eigenschaft der Zellen ist es zu verdanken, dass eine Art Blockade der Zellen geschaffen wird, die das Durchdringen der Mikroorganismen oder deren Toxine erschwert (negativer Chemo-toxismus).

Auf diese Weise ist es möglich, die Frage über Aminosäuretherapie zu stellen.

Die experimentelle Arbeit des Verfassers zusammen mit Frau Dr. Jermoljewa über "Aminosäuretherapie der Vogel malaria" hat ergeben, dass Alanin einen viel leichteren Verlauf der Krankheit bei Kanarienvögeln hervorzurufen im Stande ist und dass eine bedeutend grössere Zahl der Tiere die Krankheit überstehen als die Kontrolltiere.

Diese Ergebnisse unterstützen bedeutend die Hypothese des Verfassers.

SCHILF, ERICH und W. FELDBERG (BERLIN). Neuere Durchströmungsmethoden am ganzen Tier. (Demonstration)

SCHLOSSMANN, H. (DÜSSELDORF). Thyroxinwirkung und Ernährung.

Die Steigerung des Sauerstoffverbrauches unter dem Einfluss von Thyroxin ist weitgehend von der Art der Ernährung abhängig, worauf schon Abelin sowie Abderhalden und Wertheimer hingewiesen haben. In Serienversuchen an weissen Ratten ergab sich, dass bei jeder Form von einseitiger

ger Ernährung die Stoffwechselwirkung des Thyroxins abgeschwächt wird. Es waren allerdings deutliche Unterschiede bei den einzelnen Ernährungsformen vorhanden.

SCHMIDT, CARL F. and A. E. LIVINGSTON (PHILADELPHIA). **Influence of Size of Dosage upon Development of Tolerance to Morphine in Dogs.**

A high degree of tolerance is only very slowly acquired when the daily dose is small (2 or 10 mgm. per kilo). As long as 3 months may be required for the development of maximal tolerance to 2 mgm. per kilo daily, and more than 4 months for the appearance of maximal tolerance to 10 mgm. per kilo daily. On the other hand, with ascending dosage, or with larger doses from the start (25 to 60 mgm. per kilo), maximal tolerance is developed much more rapidly than this. Dogs given a very large (convulsant) dose on the first day are distinctly more resistant than normals to the narcotic (but not to the gastro-intestinal) effects of 10, 30, or 60 mgm. per kilo upon the next day, and on daily administration of the same dose uniformly survive to become maximally tolerant in a much shorter time than is possible with any other regime of dosage. The rapidity with which tolerance is acquired therefore seems to depend upon the concentration of morphine in contact with the tissues. But once tolerance has been acquired to 2 or 10 mgm. per kilo daily, the tolerance prevents the narcotic effects of 100 mgm. per kilo, though the larger dose elicits marked gastro-intestinal effects. Morphine tolerance appears to depend chiefly upon a cellular resistance or immunity, which is objectively demonstrable in blood vessels and medullary centers.

SCHMITT, FRANCIS O. (BERLIN-DAHLEM). **The Gaseous Metabolism of Nerves During and Following Anaerobiosis.**

Using differential manometers and a new type of vessel, both the oxygen consumption and the CO₂ production of nerves have been measured upon the same nerves. That nerves incur an oxygen debt in asphyxia has been confirmed and the effect of stimulation and of chemicals upon this debt studied. By refinement of technique, the respiratory quotient of the first hour of recovery respiration following anaerobiosis has been measured and found to lie between 0.53 and 0.60 or somewhat lower than the respiratory quotient of resting metabolism. The CO₂ production has been determined for varying periods of rest and of stimulation in nitrogen. Although individual variations from one set of nerves to the next render it difficult, a curve representing the CO₂ production during asphyxia has been constructed from these single observations made from 1 to 24 hours after placing the nerves in nitrogen.

SCHMITZ, ERNST und FELIX KOCH (BRESLAU). **Über qualitative Veränderungen der Plasmaphosphatide bei der Aderlasslipämie der Kaninchen.**

Es ist eine seit langem bekannte Tatsache, dass im Verlauf grösserer Aderlässe die Gerinnbarkeit des Blutes wächst. Diese Veränderung ist nicht an eine Zunahme des Fibrinogens gebunden, wird vielmehr auf einen Zustrom von Gewebsflüssigkeit zum Blutplasma zurückgeführt. Vom Standpunkt der einzelnen Gerinnungstheorien aus werden die dem Blut aus den Geweben zufließenden Agentien verschieden benannt, es besteht aber Einigkeit darüber, dass es sich hier um freie oder an Eiweiss gebun-

dene Lipide handelt. Unter diesen ist es, wie zuerst von Howell festgestellt wurde, das Phosphatid Kephalin, an dem die gerinnungsfördernde Wirkung haftet. Da die Phosphatide Lecithin und Kephalin sich nur durch die Methylierung der Aminogruppe der Base unterscheiden und da, wie wir wissen, der Organismus Methylgruppen sowohl einzuführen, als wegzunehmen vermag, erscheint es möglich, dass das Mengenverhältnis beider Phosphatide durch experimentelle Massnahmen verändert werden kann. Es wurde am Beispiel der Aderlasslipämie der Kaninchen, bei der die erhöhte Gerinnbarkeit des Blutes zu einer dauernden Eigenschaft wird, untersucht, ob hier eine Verschiebung des Verhältnisses Lecithin: Kephalin die absolute Mengenzunahme begleitet. Zu diesem Zweck wurde ein Verfahren ausgearbeitet, die Phosphatide von den übrigen stickstoffhaltigen Plasmabestandteilen zu trennen und ihre Gesamtmenge sowie den Anteil des Kephalins zu bestimmen. Zur Messung des Aminostickstoffs wurde das kolorimetrische Verfahren nach Folin herangezogen, da die Mengen für die gasometrische Bestimmung nach Van Slyke zu klein waren. Die Versuche ergaben, dass im Verlauf der Aderlasslipämie nicht nur ein Anstieg der gesamten Phosphatide, sondern manchmal auch ein Überwiegen des Kephalins über das Lecithin hervortritt. Die Konzentrationen des Kephalins kämen nahe an die von Waksman als das Optimum für die Gerinnung ermittelten heran. Die Aderlasslipämie geht danach mit einer qualitativen Veränderung des Phosphatidkomplexes im Blutplasma einher, die geeignet ist, zur Erhöhung der Gerinnbarkeit beizutragen. Der reichliche Zustrom von Gewebsflüssigkeit zum Plasma dürfte eines der Momente sein, die zum Zustandekommen der Lipämie beitragen.

SCHNEIDER, EDWARD C. and GORDON C. RING (MIDDLETOWN, CONNECTICUT). **The Influence of a Moderate Amount of Physical Training on the Respiratory Exchange and Breathing during Physical Effort.**

Physical work for an hour a day increased the load-carrying ability within one week, but it required from 5 to 7 weeks to produce the maximum result. A let-down in the regularity or amount of daily work soon reduced the load-carrying ability, but even with complete neglect of exercise some of the gain in power was maintained for several months.

The increase in the percentage of carbon dioxide exhaled and of oxygen absorbed was maximal within from 4 to 5 weeks. Each of these returned to the pre-training level soon after the discontinuance of training.

A decrease in the respiratory quotient of work during training suggests a gain in ability to more adequately reconvert lactic acid into its precursor.

SCHRIEVER, HANS (WÜRZBURG). **Untersuchungen über die elektrische Erregbarkeit der Sinnesnerven.**

Bei Untersuchung der einzelnen Sinnesnerven mit kurzen Stromstößen zeigt sich insofern eine Einheit der Reizgesetze als bei Verwendung von Kondensatorentladungen fast überall in erster Annäherung das Hoorweg'sche, bei Verwendung sog. rechteckiger Stromstöße das Weiss'sche Gesetz gilt. Die unterschiedliche Wirkung des kontinuierlichen Stroms (Gültigkeit des Pflügerschen Erregungsgesetzes, Möglichkeit des Einschleichens usw.) erklärt sich demgegenüber dadurch, dass dieser nicht nur direkt, sondern bei einzelnen Sinnesnerven auch noch auf dem Wege über elektrolitische Zersetzungsprodukte in den Geweben chemisch reizend wirkt.

Es folgen dann nähere Ausführungen über den Stärke- und Zeitbedarf der einzelnen Sinnesnerven an Strom, wobei als wichtigstes hervorzuheben ist, dass beide im Grunde unabhängig von einander sind, insofern als sich für beide eine völlig andere Rangordnung der Sinnesnerven ergibt, und bei verschiedenen Funktionszuständen beide sich im entgegengesetzten Sinn ändern können. Eine nähere Beschreibung der Versuche erfolgt in der Zeitschrift für Biologie.

SCHULTZ, W. H. (BALTIMORE). **A Quantitative Study of Human Adrenals. 1. Is it Possible to Have a Hyperfunction of Adrenal Tissue Comparable to the Hyperfunction Known to Exist in the Thyroid Gland?**

Improved methods for assaying biologically and colorimetrically were used in studying quantitatively fresh human adrenal glands. An extensive study was made of a tumor of the adrenal gland removed from a patient diagnosed as "accessory adrenal" by virtue of the periodic hypertension amounting to as much as 260 mm. blood pressure. Extracts of this tumor compared with other fresh adrenal extracts revealed an unusually rich adrenalin content. Quantitative analyses will be presented and the results discussed in connection with blood pressure measurements made upon the patient before and after removal of the tumor.

SCOTT, F. H. and R. N. BIETER (MINNEAPOLIS). **Blood Pressure and Plasma Protein Determinations in the same Frog.**

If the glomerulus of the kidney acts as a mechanical filter, there must be sufficient blood pressure in the glomerular capillaries to overcome the osmotic pressure of the colloids of the blood. While one may find in the literature data on the osmotic pressure of the blood colloid and of blood pressure in the frog, none of these pertain to the same frog. It was therefore felt desirable to determine the blood pressure and the colloid on the same frog. For this purpose an apparatus, which will be demonstrated, was devised. It is essentially a small apparatus such as is used for taking blood pressure in man. The rubber bag was wrapped around the leg and the vessels observed under the microscope in the foot. The accuracy of the method was checked by inserting a cannula into the coeliac artery and recording the pressures there by means of a Hürthle, Harvard or mercury manometer. The pressures of each frog were read for a number of days, after which they were bled either through a cannula in the coeliac artery in the case of large frogs or from the heart. A small injection of heparin was given subcutaneously about one-half hour previous to the bleeding. The blood was centrifuged and the protein content of the plasma determined by precipitating with trichloroacetic acid, washing and drying at 102°. Hayman showed that glomerular pressure is about 54 per cent of systolic aortic pressure. Our results show that in the frog, using this factor of Hayman, there is always sufficient glomerular pressure to overcome the osmotic pressure of the colloid.

SCOTT, F. H. and R. N. BIETER (MINNEAPOLIS). **Apparatus for Determining Systolic and Diastolic Pressures in the Normal Frog. (Demonstration)**

SCOTT, J. M. DUNCAN (SASKATOON). **The Structure of Ferric Hydrosol.**

From a comparison of the amounts of various di- and tri-valent ions required for the precipitation of different preparations of ferric hydrosol a hypothesis is suggested as to the general type structure of this colloid.

SCOTT, J. M. DUNCAN (SASKATOON). **A Commentary on Listing's Law. (Demonstration)**

If a sphere is rotated through an angle B around an axis inclined at an angle A to the perpendicular which otherwise conforms to the requirements of Listing's Law (*i.e.*, "is situated in the coronal plane") the restoration angle G through which the sphere must be rotated around the original "antero-posterior" axis in order to restore to the vertical the meridian which was zero vertical with respect to the original perpendicular axis (and which is a great circle with respect to the new oblique axis) is given by the family of curves:

$$G = - \left[\text{angle } A - \arccos \left\{ \frac{\cos A \cdot \cos B}{\sqrt{1 - \cos^2 A \cdot \sin^2 B}} \right\} \right]$$

Either this complicated law must be followed by the neuro-muscular apparatus of the eye or the restoration of what was the zero vertical meridian to a vertical position when the visual axis is directed into any quadrant of the field of vision must be incomplete. When the after-image of a right cross is projected into any of the four quadrants of the field of vision its limbs are not truly vertical and horizontal, the reason being that the neuro-muscular apparatus does not conform to the mathematical equation.

The model on which the family of curves was originally worked out is exhibited.

SCOTT, J. M. DUNCAN (SASKATOON). **The Ponto-Bulbar Vasomotor Centre. (Demonstration)**

With a Clarke's stereotaxic instrument carrying a capillary electrode for extremely weak unipolar stimulation the brain stems of decerebrate cats have been searched for the vasomotor centre. The results have been controlled by observing the electrical changes shown by the most reactive spots when rise of blood pressure is produced reflexly.

The method of use of the instrument, some typical tracings and sections will be demonstrated.

SEAGER, L. D. and W. E. BURGE (URBANA, ILLINOIS). **Evidence that the Heart Uses Alcohol in Preference to a Meat Digest or Amino Acids.**

Four hearts were removed from turtles and the coronary vessels were washed for twenty minutes by inserting a cannula into the arch of the aorta and forcing Locke's solution through these vessels. Each heart was then attached to a perfusing apparatus and perfused with the following solutions for ten hours: 25 cc. of Locke's solution to which 25 mgm. of aminoids (meat digest) had been added; 25 cc. of Locke's solution to which 25 mgm. of a mixture of the sodium salts of the following amino acids had been added: glycine, alanine, *l*-leucine, *dl*-valine, *l*-cystine, *d*-glutamic acid, *l*-histidine, *l*-tyrosine, *l*-tryptophan, *dl*-phenylalanine, *l*-aspartic acid, and arginine; and 25 cc. of Locke's solution to which 25 mgm. of aminoids and 0.15 cc. of 100 per cent ethyl alcohol had been added. The

amino acid content of the solutions as well as the alcoholic content was determined at the end of the experiment after ten hours. Van Slyke's method was used for determining the amino acids, and the iodoform test for the alcohol.

The following is the average for a series of six experiments. The hearts that were perfused with Locke's solution plus the aminoids used 26 per cent of the aminoids in 10 hours; those perfused with Locke's solution plus the amino acids used 17 per cent of the amino acids; those perfused with Locke's solution plus the aminoids and 0.15 cc. of alcohol used only a trace of the aminoids and all the alcohol; those with 0.5 cc. of alcohol used none of the aminoids; those perfused with Locke's solution and 0.15 cc. of alcohol also used all the alcohol.

From the preceding it will be seen that the isolated turtles' hearts used amino acids when alcohol was not present but that when it was present they used the alcohol instead.

SEAGER, L. D., E. WILLIAMS and W. E. BURGE (URBANA, ILLINOIS).

A Study of the Stimulating Effect of the Excretions on Metabolism.

The excretions used were the urine, certain of its constituents and carbon dioxide. Eight hundred cubic centimeters of 0.1 per cent dextrose solution were prepared and divided into 100 cc. portions. Each portion was introduced into a beaker and two goldfish of approximately the same size and with a combined weight of approximately 5 grams were introduced into each beaker. Air was bubbled through the solutions to insure an adequate supply of oxygen to the fish. One cubic centimeter of sterilized urine was added to one beaker; the ash from 1 cc. of urine was added to another; the phosphate precipitate from 1 cc. of urine to another; the filtrate from the phosphate precipitate to another; 100 mgm. of sodium chloride to another; 50 mgm. of di-potassium phosphate to another; carbon dioxide together with oxygen was bubbled slowly through the sugar solution in another beaker, and the remaining beaker to which nothing was added served for control. Sugar determinations were made immediately and after twenty-four hours, at the end of the experiment, according to the method of Benedict. The following is the average of six series of experiments. The control fish used 28 per cent of the sugar in 24 hours; those to which 1 cc. of sterilized urine was added used 56 per cent of the sugar; those to which the ash of the urine was added used 48 per cent of the sugar; those to which the phosphate of the urine was added used 45 per cent of the sugar; those to which the filtrate from the phosphate precipitate was added used 32 per cent of the sugar; those to which the di-potassium phosphate was added used 46 per cent of the sugar; those to which the urea was added, 34 per cent and those to which the carbon dioxide was administered used 29 per cent of the sugar.

From the preceding it may be seen that carbon dioxide had no effect on sugar utilization; that the urine, as well as its ash and the phosphates increased sugar utilization; that the urine lost most of its stimulating effect when the phosphates were removed and that the phosphate precipitate stimulated sugar utilization almost as much as the urine itself. The conclusion is drawn that the stimulating effect of urine on sugar utilization is due principally to the phosphates.

SEEL, HANS (HALLE A.D. SAALE). Ueber die Bildung toxischer Umwandlungsprodukte des Ergosterins bei Ultraviolettbelichtung.

Klinische Befunde und ausgedehnte eigene experimentelle Untersuchungen über das synthetische antirachitische Vitamin "D" legten die Frage nahe, ob bei der Bestrahlung des Ergosterins toxische Umwandlungsprodukte entstehen können. Wurde Ergosterin in Substanz oder in alkoholischer Lösung mit einer künstlichen Höhensonne "Hanau" unter Luftzutritt 1 bis 20 Stunden bestrahlt, so veränderten sich sowohl die Lösungsverhältnisse wie der Schmelzpunkt des Ergosterins. Allmählich ging es aus der kristallinen Form in eine gelb-grüne, harzige Masse über und reagierte deutlich sauer. Durch Behandlung mit n/10 NaOH bis zum Neutralpunkt ging ein Teil der Substanz in klarer Lösung; durch Zusatz entsprechender Menge n/10 HCl wurde es wieder ausgefällt und durch Aetherextraktion isoliert. Im Tierversuch erwiesen sich diese Substanzen als ziemlich giftig. Sie bewirkten Hämolyse roter Blutkörperchen, systolischen Herzstillstand, lokale Nekrose der Gewebe, Gewichtsverlust, Fressunlust der Tiere und Nierenschädigungen bei intravenöser Einverleibung (Kaninchen). Auch auf pflanzliches Eiweiss (Blumen und Samenversuche) wirken diese Umwandlungsprodukte giftig. Ein Antirachitische Wirksamkeit war nicht mehr nachzuweisen. Die biologischen Wirkungen dieser Substanzen sind denjenigen der saueren Oxydationsprodukte des Cholesterins, wie sie früher von Flury und Seel beschrieben worden sind, durchaus ähnlich. Auch bei der Bestrahlung des Cholesterins liessen sich ähnliche Umwandlungsprodukte auf biologischen Wege nachweisen.

Eine chemische Isolierung dieser Umwandlungsprodukte war aus Mangel an Material bisher nicht möglich; jedoch sprechen die pharmakologischen Befunde dafür, dass die unter oben genannten Bedingungen bei der Belichtung des Ergosterins und Cholesterins entstehenden Umwandlungsprodukte der Gruppe der Gallensäuren und Saponine zuzurechnen sind.

SENDROY, JULIUS, JR., S. H. LIU and DONALD D. VAN SLYKE (NEW YORK).

The Gasometric Estimation of the Relative Affinity Constant for Carbon Monoxide and Oxygen in Whole Blood at 38°C.

In the course of an investigation of the arterial blood oxygen tension in man, the carbon monoxide method of Haldane and Smith was used. This method involves the law finally formulated by Douglas, Haldane and Haldane, expressed mathematically by the equation

$$\frac{[\text{HbCO}]}{[\text{HbO}_2]} = K \frac{p_{\text{CO}}}{p_{\text{O}_2}}$$

where the brackets indicate concentrations of hemoglobin in union with gas, p_{CO} and p_{O_2} the gas tensions, and K the relative affinity constant for hemoglobin for the two gases.

Undiluted, hemolyzed ox blood and human blood were saturated with various gas mixtures until equilibrium was attained. Two methods of saturation were employed, one a closed system, the other open to the atmosphere. The CO hemoglobin and oxyhemoglobin were estimated gasometrically according to Van Slyke and Neill and Van Slyke and Rabscheit-Robbins. Oxygen tension was obtained by analysis. CO tension was accurately made up and the result calculated.

Up to the present time, three normal and three pathological bloods

studied indicate for thirteen separate experiments, an average value of 210 for K. Fifteen experiments on ten different ox bloods give an average value of 179 for K. These values are tentative, subject to a correction, which would not change the order of magnitude. All results are within ± 2.5 per cent of the average. We have so far found no individual variation within the species in K for either ox blood or human blood, exceeding the limit of experimental error.

SERENI, ENRICO (NAPOLI). **Correlazioni umorali nei Cefalopodi.**

E' solo negli ultimissimi anni che il problema della esistenza o meno di correlazioni umorali in animali diversi dai Vertebrati è stato saggiato sperimentalmente: e nessuna ricerca è stata per ora eseguita nei Molluschi ed in particolare sui Cefalopodi.

Da oltre due anni ho iniziato l'analisi sperimentale del problema in questi ultimi animali; nei quali, per la loro elevata e complessa organizzazione, era più ragionevole attendere risultati positivi. In effetto, e per quanto le ricerche siano tuttora in corso di esecuzione e di sviluppo, i risultati ottenuti mi consentono già oggi di rispondere al quesito fondamentale; e mi pongono in condizione di affermare l'esistenza nei Cefalopodi di fenomeni di correlazione umorale.

Tra i dati di fatto riuniti a sostegno di questa affermazione si possono ricordare i seguenti:

1) Il tono di molti centri nervosi (ed in particolare quello dei centri che presiedono alla colorazione) è sicuramente condizionato da fattori umorali, come ho potuto dimostrare in vario modo, e tra l'altro per mezzo del preparato di circolazione crociata da me ideato.

2) Il fattore, o i fattori umorali che partecipano al mantenimento del tono dei centri nervosi sopraindicati sono assai probabilmente in rapporto con l'attività delle ghiandole salivari posteriori. Ai diversi argomenti indiretti che stanno a favore di questa ipotesi ho potuto aggiungere l'esito della estirpazione delle ghiandole suddette: dopo la quale il tono dei centri indicati diminuisce progressivamente fino alla morte.

3) I caratteri sessuali secondarii (ectocotile) sono determinati in via umorale, come è dimostrato dall'esito della castrazione, praticata sia nei maschi che nelle femmine.

Le ricerche sono state eseguite principalmente su *Octopus vulgaris* e *Macropus* e su *Eledone moschata*; ma anche su altre specie. Sono in corso di esecuzione esperimenti su altri organi.

SERENI, ENRICO e LIVIA GAROFOLINI (NAPOLI). **Anafilassi nelle colture di tessuti in vitro.**

La tecnica delle colture dei tessuti in vitro è stata a più riprese utilizzata per lo studio dei fenomeni immunitari; ma solo poche volte essa ha trovato impiego nell'esame dei problemi dell'anafilassi.

Abbiamo perciò studiato i fenomeni dell'anafilassi attiva e passiva in colture di tessuti di embrione di pollo. Abbiamo preferito le colture di questo animale perchè, mentre da un lato è noto che esso presenta i fenomeni dell'anafilassi, dall'altro la tecnica delle colture è nei suoi riguardi assai più perfetta e meglio conosciuta.

I risultati principali delle ricerche si possono riassumere brevemente come segue:

1. E' possibile, coltivando in vitro i tessuti di un animale sensibilizzato, provocare i fenomeni dello scatenamento con l'aggiunta al terreno di coltura dell'antigene. I risultati ottenuti in questo caso servono anzi come controllo e paradigma dei fenomeni dello scatenamento.

2. Se si coltivano in plasma normale con aggiunta di antigene i tessuti di un animale nuovo, la sensibilizzazione (attiva) riesce soltanto con la milza ed il midollo osseo. Tutti gli altri tessuti non si lasciano cioè sensibilizzare attivamente, almeno in vitro.

3. Tutti i tessuti, compresi naturalmente la milza ed il midollo osseo, si lasciano invece sensibilizzare passivamente, quando siano coltivati in plasma di animale sensibilizzato (o in plasma normale con antigene, quand si pratici la coltura affrontata con la milza).

4. La comparsa della sensibilità attiva nelle colture di milza è precocissima; e questo fatto, connesso con quello che si è detto sulla capacità degli altri tessuti ad essere sensibilizzati soltanto passivamente, consente di spiegare il periodo della incubazione, in vivo, come quello durante il quale gli anticorpi prodotti in alcuni tessuti si distribuiscono in tutti gli altri fino a raggiungere, in particolar modo nei "tessuti dello choc," la concentrazione necessaria.

SHAFFER, P. A., BEN K. HARNED and WM. B. WENDEL (ST. LOUIS).
Further Studies on Antiketogenesis: The Oxidation of Acetoacetate, Induced by Air Oxidation of Sugars, and by Aeration of Tissue Suspensions.

Earlier experiments showed that acetoacetate undergoes oxidation in simple solution when glucose and other sugars are being simultaneously oxidized by H_2O_2 . This "ketolytic" effect of sugar oxidation was regarded as perhaps analogous to the antiketogenic action of carbohydrate in human metabolism. The high alkalinity of caustic alkali employed and the use of H_2O_2 as the oxidizing agent made the analogy remote. It is now found that air or O_2 is effective; and with sugars like dihydroxyacetone which are oxidizable by oxygen at low alkalinity, the induced oxidation of acetoacetate occurs within physiological range of pH. These facts render the view somewhat more plausible that this and other oxidations may be similarly induced by sugar oxidation in living cells. Results of new experiments with aerated tissue suspensions lend some support to this view.

Evidence will be reported concerning the mechanism of the induced reactions; they appear to depend upon the primary formation of sugar peroxides (or of peroxides of sugar-acceptor complexes). The probable existence of such *substrate* peroxides has an important bearing upon the validity of current interpretations of biological oxidations as "dehydrogenation." "Dehydrogenases" probably do *not* "dehydrogenate," but rather activate by "dehydrogen-ion-ization" and consequent exposure of valence electron pairs.

SHAFFER, P. A. (ST. LOUIS). **Methods for the Electrometric Determination of Sugar in Blood Filtrates and Other Solutions. (Demonstration)**

SHAFFER, P. A. and M. SOMOGYI (ST. LOUIS). **Copper-Iodometric Methods of Sugar Analysis. (Demonstration)**

- a. Macro and micro blood sugar determinations.
- b. Determinations in urine and other solutions.

SHAMBAUGH, NOEL F., ED. J. D. DOTY and CYRUS C. STURGIS (ANN ARBOR). **Comparison between the Toxicity of Cystine, Tyrosine and Phenylalanine.**

White rats on a basic diet were given *per os* administrations of cystine, tyrosine and phenylalanine by esophageal catheter. Bi-daily doses of such amounts were given that a total of three milligrams per gram of body weight was received daily by each animal. The amino acids were to some groups given unneutralized, suspended in physiological sodium chloride solution. To other groups the substances neutralized by the theoretical amounts of sodium hydroxide were given in physiological saline solution. The animals were sacrificed after five, ten and in some instances fifteen days of the above regime. Both kidneys and a portion of the liver tissue were removed for histological examination.

Cystine was found to produce the greatest degree of damage both hepatic and renal. The renal damage occurred principally in the tubular areas. The hepatic pathology consisted of perilobular fibroblastic proliferation as well as retrograde change in the parenchyma.

Tyrosine produced damage principally to the renal glomeruli in contrast to the tubular damage by cystine. The liver changes with tyrosine, though definitely present, were less marked than those observed following cystine administration.

Phenylalanine was found to be the least toxic. The pathology in the liver and kidney after large doses over short time periods was found to be indeterminate in contradistinction to that observed following cystine and tyrosine administration.

SHAW, L. A. and L. T. FAIRHALL (BOSTON). **A Method for Measuring the Cutaneous Respiration in Man. (Demonstration)**

SHEAR, M. J., MARTHA WASHBURN and BENJAMIN KRAMER (BROOKLYN). **Serum Calcium; Undersaturation vs. Supersaturation.**

In a paper presented at the XIIth International Physiological Congress, Warburg¹ concluded "Es ist unsicher, ob das Plasma normalerweise mit Ca^{++} gesättigt ist, unwahrscheinlich aber ist es, dass es damit übersättigt ist."

No explanation has as yet been advanced which accounts satisfactorily for the concentration of calcium in blood serum. In spite of numerous studies, this question has not been solved; the recent elaborate physico-chemical studies, instead of clarifying the situation, have only added to the existing perplexities.^{2, 3, 4}

In a previous communication⁵ we presented evidence which indicated that serum does not contain abnormal amounts of calcium and that serum is not supersaturated. Furthermore, the important substance appears to be CaHPO_4 and not $\text{Ca}_3(\text{PO}_4)_2$.

The present paper summarizes the results obtained by shaking inorganic serum solutions with crystalline CaHPO_4 . These solutions had the same

¹ E. J. Warburg. Biochem. Zeitschr., 1926, clxxviii, 208.

² L. Emmett Holt, Jr., Victor K. La Mer and H. Bruce Chown. Journ. Biol. Chem., 1925, lxiv, 509, 567.

³ L. Emmett Holt, Jr. Journ. Biol. Chem., 1925, lxiv, 579.

⁴ Julius Sendroy, Jr. and A. Baird Hastings. Journ. Biol. Chem., 1927, lxxi, 783, 797.

⁵ M. J. Shear and Benjamin Kramer. Journ. Biol. Chem., 1928, lxxix, 125.

inorganic composition as normal blood serum; they were of constant composition as regards all the constituents except calcium and phosphorus. The concentration of these latter constituents was varied from 0 to 10 mgm. per 100 cc. in such a way that the $\text{Ca} \times \text{P}$ products varied from 0 to 65. Some solutions contained high calcium and low phosphorus concentrations; others contained the reverse.

When these serum solutions were shaken with CaHPO_4 , equilibrium was reached in 1 hr. After equilibration, the ion product $[\text{Ca}^{++}] \times [\text{HPO}_4^{--}]$ in all these solutions was identical. Shaking with CaHPO_4 had caused an *increase* in the concentration of calcium, or of phosphorus, or of both, in all solutions with $\text{Ca} \times \text{P}$ products less than 45; in all these solutions the ion product after equilibration was greater than the initial value. These solutions were therefore initially undersaturated with respect to CaHPO_4 . Twenty experiments at 38° gave a value of 3.4×10^{-6} for $K'_{s.p.}$ CaHPO_4 , the solubility product of CaHPO_4 at the ionic strength of serum.

In active rickets the $\text{Ca} \times \text{P}$ product is less than 35, according to Howland and Kramer.¹ Inorganic serum solutions with $\text{Ca} \times \text{P}$ products of 35 or less are definitely undersaturated; ricketic serum would therefore appear to be undersaturated.

SHEARD, CHARLES and LOUIS A. BRUNSTING (ROCHESTER, MINNESOTA).

Optical Measurements on the Color of the Skin as Affected by Race, Environment, Radiant Energy and Superficial Blood.

Spectrophotometric measurements on the skin show that the fundamental hue or dominant wavelength is in the region 580 to 590 millimicrons, or spectral yellow. Pigment is not a racial characteristic. Pigment does not disturb the hue or purity of the color of the skin but tends to lower the values of the relative luminosity. The blood of the superficial capillaries exerts a marked influence on the reflection of light and therefore on the color of the skin. An abundance of oxygenated blood near the surface tends to shift the dominant wavelength toward the red end of the spectrum; an abundance of venous blood or stasis produces cyanosis with a shifting of the dominant wavelength toward the blue end of the spectrum. By analysis of the spectrophotometric curves into fundamental color excitation values it is possible to differentiate changes due to separate or combined alterations in the content of blood and of pigment, as produced by radiant energy or by other factors of a normal or pathological character.

SHEARD, CHARLES and GEORGE E. DAVIS (ROCHESTER, MINNESOTA).

Investigations on Bile Pigment, Purified Bilirubin and Blood by Ultraviolet Spectrophotometry.

Ultraviolet spectrophotometry has been employed in investigations on the absorption curves and the "fading" of solutions of sodium bilirubinate and of naturally formed bilirubin in serum with and without dilution in various solvents. Transmission curves for bilirubin dissolved in sodium hydroxide and sodium bilirubinate in human serum show a maximal absorption at 432 millimicrons. Tests on the fading phenomenon of bilirubin indicate that undiluted serums fade comparatively slowly, but that other complex changes in composition occur. The absorption curve of

¹ J. Howland and B. Kramer. Trans. Amer. Pediat. Soc., 1922, xxxiv, 204.

oxyhemoglobin and the effects of hemolysis on spectrophotometric data for bilirubin have been investigated and will be discussed. A comparison of absorption spectra of serums giving the "direct" and "indirect" types of van den Bergh reaction indicate that the two types of reaction cannot be differentiated spectrophotometrically. Data have been obtained indicating that bilirubin in serum exists as such and not as some salt, such as sodium bilirubinate. Investigations in the ultraviolet spectrophotometry of bile from the gall bladder and of serums in cases of experimentally produced obstructive jaundice lead to the conclusion that one and only one pigment is developed.

SHERMAN, H. C. and H. L. CAMPBELL (NEW YORK). Further Experiments upon the Influence of Food upon Longevity.

In experiments with rats, the authors have shown that, starting with a diet already adequate, it is possible, by improving the relative proportions in which the articles of food enter into the food mixture, to induce a higher degree of health with decreased infant mortality and a prolongation of the lives of adults. Further experiments confirm and extend this finding, clarify the precision of the measurement of increased longevity, and throw some light upon the ultimate chemical factors involved.

SILBERSTEIN, F. and J. KRETZ (VIENNA). Interrelation of Spleen and Liver.

In order to gain a more definite knowledge about the reciprocal influence of the functions of spleen and liver a fistula was made between the vena lienalis and the vena cava inferior. At the same time the circulation of possibly all veins leading from the spleen to the veins of the stomach was cut off. Examinations of the blood-picture were continuously made.

In a second series of experiments it has been tested whether this operation influences the intermediate metabolism and finally it has been pointed out whether the reaction of these animals against blood-poisons is changed.

SINCLAIR, R. G. and W. R. BLOOR (ROCHESTER, NEW YORK). The Metabolism of the Phospholipids.

Although it has long been known that lipids are present in all plant and animal tissues, it is only since the extensive investigations of a group of French workers under the leadership of André Mayer that it has been realized that the phospholipids are essential cell constituents. The outstanding importance of the tissue phospholipids has been emphasized by Bloor who has suggested that the amount and the degree of unsaturation of the phospholipids of a tissue are a function of its metabolic activity.

Mayer and Schaeffer have shown that the percentage amount of ether-soluble phosphorus (that is, the phospholipids) in animal tissues is quite independent of the state of nutrition of the animal. Recently Terroine and Belin have come to the conclusion that the *composition* of the phospholipids is likewise independent of the nutritional condition of the animal and of the type of diet fed. Evidence obtained in this laboratory shows that such is not the case.

We have found that the type of diet fed to cats over a considerable period of time exerts a distinct and uniform influence on the degree of unsaturation of the phospholipid fatty acids in the intestinal mucosa, liver, heart, kidney, and smooth and skeletal muscle. The brain alone seems to be an

exception to the rule. Furthermore we have shown that the composition of the phospholipids of whole rats is dependent on the diet of the animals. This influence of diet on the composition of tissue phospholipids seems to indicate that, as a result of the metabolic activity of the tissues, the phospholipid constituent of the protoplasm is subject to continual wear and tear, in the repair of which the fatty acids of the circulating lipids are utilized.

Besides the gradual influence exerted by diet as a result of the wear and tear of tissue phospholipid, we have found that the ingestion of a characteristic fat (such as cod liver oil) produces an immediate effect on the composition of the phospholipids of the intestinal mucosa, and the liver. It is believed that the evidence shows that phospholipid in these organs is involved in the absorption and assimilation of fat.

SMITH, ARTHUR H. and PEARL P. SWANSON (NEW HAVEN). Blood Changes Induced by Diets Defective in Inorganic Constituents.

It has been demonstrated¹ that cessation of growth and maintenance of body weight can be produced in very young rats by feeding rations con-

Comparison of certain blood constituents of rats, stunted by a defect in inorganic salts in the diet with those of normal rats

BLOOD CONSTITUENT	NORMAL RATS		STUNTED RATS	SIGNIFICANCE RATIO	
	Physiological controls	Chronological controls		Stunted rats and physiological controls	Stunted rats and chronological controls
Erythrocyte count in millions.....	7.7 ±0.79	9.7 ±0.79	12.0 ±0.92	27.2	14.4
Red cell volume, per cent. 48	±2.41	54 ±3.04	45 ±2.07	6.6	16.4
Hemoglobin, gms./100 cc.....	15.4 ±1.77	17.4 ±1.40	14.3 ±1.70	3.4	10.7
Total solids, per cent.....	19.3 ±1.32	20.6 ±1.68	18.9 ±2.1	1.0	4.4
Plasma protein nitrogen gms./100 cc. pl.....	1.01 ±0.065	1.14 ±0.07	1.06 ±0.106	2.97	4.5

taining minimal concentrations of inorganic salts. In the present study a similar condition has been induced in larger rats; sufficient blood could thus be obtained to permit a chemical and morphological study. When normal animals weighing 120 grams are given the experimental diet which contains only 0.5 per cent ash, they continue to grow for about 30 days until they reach a body weight of 160 to 170 grams which weight is maintained throughout the experimental period (90 days). Two control groups of normal animals were studied simultaneously; the first, consisting of rats of the same body weight as the experimental group and the second, made up of animals of the same age.

A sufficient number of animals was studied to permit statistical treatment of the data derived. The results are summarized in the accompanying table. There is a marked and significant increase in the erythrocyte count of the blood of the experimental group over the values of both types of control animals. There is a significant decrease both in red cell volume and in hemoglobin concentration in the blood of the experimental rats

¹ Winters, J., Smith, A. H., and Mendel, L. B., *Am. Jour. Physiol.*, 80, 576, 1927.

when compared to either of the control groups. At the same time the blood total solids of the experimental rats are lower than the value for the control animals of the same age though not significantly different from the controls of the same body weight. The plasma protein nitrogen of the blood of the stunted rats is less than that of the controls of the same age but not significantly different from that of the normal rats of the same weight.

The experimental evidence indicates that the dietary adjustment employed in this study results in the production of (I) a true polycythemia, (II) erythrocytes with a diminished concentration of hemoglobin, (III) red cells of smaller size than normal and, (IV) water and plasma protein concentrations typical of a normal animal of the same weight rather than of the same age. The picture, on the basis of the studies thus far completed is that of an infantile blood with a relatively enormous overproduction of small, anemic red cells.

SMITH, FRED M. and GEORGE H. MILLER (IOWA CITY). **A Study of the Reflex Influence of the Colon, Appendix, and Gall Bladder on the Stomach.**

There is a considerable difference of opinion relative to the possible reflex influence of the colon on the stomach. Epigastric pain, nausea, and vomiting are frequently associated with chronic colitis. Clinicians and roentgenologists have been inclined to attribute these symptoms to a disturbed motor function of the stomach induced by a reflex stimulation from the colon. The experimental investigation of this problem, however, has led to varying conclusions.

In the present investigation, dogs anesthetized by barbitol were employed. A midline incision was made in the upper abdomen which would permit exposure of the stomach and proximal colon. The stomach was filled with warm water and the activity observed during a control period. An irritant, as croton oil was introduced into the proximal colon, and air was introduced to cause moderate distention. Precautions were taken to prevent the irritant coming in contact with the ileum. Following the distention or the introduction of the irritant into the colon, there was usually a marked increase in the activity of the stomach. The peristaltic waves were much more frequent, deeper and at times, very violent. During the height of the increased activity, reverse waves were often noted. The increased activity of the stomach induced by the stimulation of the colon was abolished by atropine.

In experiments in which the croton oil was confined to the appendix there was an increase in the activity of the stomach similar to that observed following the irritation of the colon. This reflex stimulation of the stomach was also abolished by atropin.

In further experiments the reflex connections between the gall bladder and stomach was studied. The animal was prepared and the stomach exposed as in the preceding studies. A small incision was made in the fundus of the gall bladder and the bile aspirated. The remaining bile was removed by means of cotton pledgets. Croton oil was then applied to the mucous membrane of the gall bladder by a cotton swab. Within a few minutes there was usually a striking increase in the activity of the stomach comparable to that noted in the previous experiments and the results following the administration of atropin were identical.

The effects of the stimulation of the colon on the stomach were then correlated with the clinical findings in patients with spastic colitis. Pa-

tients were selected with a spastic condition of the colon who complained of epigastric distress.

This distress was localized in the epigastrium, frequently appeared 1 or 2 hours after meals and was associated with bowel symptoms. This epigastric distress was readily induced by the inflation of the stomach or distension of the colon, and immediately relieved by reducing the pressure in these locations. A rubber balloon was passed into the pyloric portion of the stomach and the location verified by fluoroscope. The balloon was filled with water and connected with a kymograph. The activity of the stomach was recorded during a control period. The colon was then inflated through a rectal tube. There was an immediate increase in the tone and activity of the stomach and the appearance of the epigastric distress. The epigastric distress was coincident with the peristaltic waves. Following the intermuscular administration of atropin gr. 1/50. There was a gradual reduction in the tone and size of the peristaltic waves with the disappearance of the pains. Further distension of the colon had no effect on the stomach and the epigastric pain was not induced.

SMORODINZEW, I. A. et A. N. ADOVA (Moscou). **Sur la nature des protéases.**

D'après la théorie d'Hugounenq et Loiseleur, l'action exercée par les protéases sur les matières albuminoïdes dépend de la présence dans leur molécule de groupes COOH et NH_2 . Désirant vérifier ce fait expérimentalement nous avons entrepris une étude physico-chimique des propriétés d'une série de préparations de pepsine. Nous avons pu établir au cours de ces études qu'il existait un parallélisme déterminé entre la teneur en azote total, $\text{NH}_2\text{-N}$, les groupes carboxyles et surtout le coefficient NH_2/COOH d'un côté, et l'activité des pepsines (déterminée d'après le procédé Gross) de l'autre. Ensuite nous avons pu montrer que l'ordre de repartition des pepsines en groupes d'après leur effet caseinoclastique restait le même et dans le cas où l'on évalue l'activité digestive de ces mêmes corps à l'égard de divers protides—édestine, gélatine, fibrine, blanc d'oeuf, protéine musculaire. Nous avons aussi réussi à démontrer le parallélisme fort intéressant existant entre l'activité de la pepsine, déterminée d'après le principe de la disparition du substratum, et l'activité du même corps évaluée d'après l'accroissement des groupes carboxyles selon Willstätter. De plus on a pu constater que la quantité des acides aminés dans les produits de la digestion n'augmentait pas pendant l'hydrolyse des différentes matières albuminoïdes par les pepsines de groupes différents et que l'on avait seulement une hausse du pourcentage des groupes carboxyliques des peptides évaluée selon Willstätter. Finalement nous avons pu noter que comparativement, à en juger d'après les groupes carboxyliques, les préparations de pepsine que nous avons étudiées manifestent un pouvoir hydrolysant plus prononcé envers la caséine qu'envers la gélatine.

SNAPPER, I. and A. GRÜNBAUM (AMSTERDAM). **Excretion of Lactic Acid During Sport.**

Different games cause different excretion of lactic acid.

A. Association football: Duration two periods of three quarters of an hour (Olympic games).

1. Warm days: Of 55 players six excreted more than 60 mgm. lactic acid in the urine.

2. Cold days: Of 32 players sixteen excreted more than 60 mgm. lactic acid in the urine.

On account of this difference between the excretion of lactic acid on warm and cold days the question was raised whether perhaps on warm days the lactic acid leaves the body in another way than through the urine. Therefore the shirts of 68 players were examined after the match and considerable amounts of lactic acid and chlorine were found. The average per shirt amounted to 460 mgm. lactic acid and 846 mgm. chlorine. The total excretion is of course much greater.

B. Rowing: Distance 2 km. (Olympic games). Duration $6\frac{1}{2}$ to 8 minutes. Thirty-nine rowers examined: 28 excreted in the urine over 60 mgm. lactic acid, one over 1 gram lactic acid. Only small amounts of lactic acid and chlorine (on an average 97.5 mgm. lactic acid and 84 mgm. Cl) were found in the shirts.

C. Running: 1. 3 km. in about 9 minutes (non-Olympic races). Of 5 runners one had more than 60 mgm. lactic acid in the urine.

2. 5 km. ($14\frac{1}{2}$ minutes) and 10 km. ($30\frac{1}{2}$ minutes).

Traces of lactic acid were found in the urine of three runners examined. However 220 and 440 mgm. lactic acid, and 616 and 877 mgm. chlorine were found in the shirts of the two 10 km. runners.

3. Marathon runners: 42 km. in about $2\frac{1}{2}$ hours. Less than 50 mgm. lactic acid were excreted in the urine by the 7 runners examined.

D. Swimming: 1. Water polo: Twice $7\frac{1}{2}$ minutes. Forty-nine players examined: 37 over 60 mgm. lactic acid in the urine (12 over 500 mgm. and 5 over 1 gram).

2. 400 m. swimming: Duration about 5 minutes. Seven swimmers examined; five over 60 mgm. lactic acid in the urine.

3. 1500 m. swimming: Duration about 20 minutes. Five swimmers examined; four excreted over 60 mgm. lactic acid in the urine, the fifth 52 mgm.

Lactic acid is nearly always excreted during sport; the amount lies usually between 1 and 2 grams. During short-timed exertions the lactic acid is excreted in the urine; during longer-timed exertions only for the smaller part through the kidney but for the greater part through the sweat (only with long-distance swimmers is there always much lactic acid in the urine. This is probably caused by impaired inspiration).

The concentration of the lactic acid in the urine can go up very high. It often exceeds 1 per cent (maximum found 2.17 per cent).

Through comparison of these figures with the analysis of the sweat of resting healthy and sick persons, it appeared that the composition of work-sweat and rest-sweat is different. During rest high lactic acid concentration (2.5-3 per cent), with lower chlorine concentration (1.60 per cent and less). During exertion low lactic acid concentrations (1 per cent with high chlorine content (2.70-3.5 per cent)).

SNYDER, CHARLES D. in collaboration with F. W. LIGHT, JR. and N. L. KALTREIDER (BALTIMORE). **Anaerobiosis and Heat Production in Smooth Muscle Organs.**

The isolated organs have been subjected to oxygen tensions definitely less than 0.001 per cent, the method not only of obtaining but also of determining the low oxygen tensions being that of Kautzky and Thiele. The behavior of the organs was studied in response to stimulation of their

motor nerves or as they contracted automatically. The responses obtained with the organs in cyanide and in "cylinder nitrogen" that had been reduced by ordinary methods, say, to 0.01 per cent of oxygen, are compared with those obtained in the absence of cyanide and with the oxygen tension reduced to less than 0.001 per cent. The behavior of the preparations with the cyanide treatment and in the higher tensions of oxygen is markedly different from their behavior in tensions of oxygen less than 0.001 per cent.

SOKOLOFF, BORIS (PRAGUE). About the Chemical Nature of the "Cancer Agent."

In his report at the International Conference on Cancer, London, 1928, Dr. James Murphy announced, that he obtained a purified extract of Rous chicken sarcoma. "This precipitate injected into chickens proved active in the production of tumors" 1.

Doctor Murphy brought out the hypothesis that malignant tumors are caused by thymus-nucleic acid. He reached this conclusion because the fraction obtained by him gives a uniform Feulgen reaction of the so-called thymus-nucleic acid group." Using the new method (made by Sharst Co., New York) of electro-dialysis apparatus I came to the following conclusions: We have no sufficient reason for either defending or denying the theory of Doctor Murphy, since it hardly could be accepted as a working hypothesis, due to the general occurrence of thymus-nucleic acid in normal tissues. We can only state that after electro-dialysis of cancer tissue the colloidal residue obtained is not uniform chemically and contains, in addition to thymus-nucleic acid, lipoids and fatty acids. On the other hand, the thymus-nucleic mass which is obtained represents in large part what is left of the destroyed cell nuclei.

SOKOLOFF, BORIS (PRAGUE). Liquefaction of Malignant Tumors and Iron Metabolism.

Some years ago, while working upon the question of metabolism of ions and their bearing upon regeneration of Protozoa, I found that adrenalin in very high dilution stimulated the catalytic action of ferric chloride, and that in infusoria high dilutions of the same substance helped to establish the nucleo-cytoplasmic ratio, thereby accelerating the regenerative processes. The cytological picture observed in these experiments resembled closely the results obtained by Khainsky in his work on the action of oxygen on *Paramoecium*.

These observations suggested the idea of applying the method of liquefaction to neoplastic tissue. Before proceeding to the main topic of my communication, it will be necessary to summarize briefly the preliminary work which I have done to ascertain the relationship existing between the function of the suprarenal glands, particularly of the cortex, and the biology of neoplasms.

Analyses of the suprarenal glands during cancer and sarcoma of different animals demonstrated to me that the cortex reacts very sensibly to malignant neof ormation; its super-activity is observed at the beginning of this neoplastic process, which later is replaced by fatty degeneration. When all the cortex (of a chicken, bearer of Rous sarcoma) is filled with the fatty incorporations the weight of the suprarenal gland is three or four times greater than normal. But especially demonstrative are the troubles of the iron incorporations.

Availing myself of the above investigations, I have performed tests with different tumors. For that purpose I have employed the preparations of Corferrol (by Sharit Chemical Co.) which constitute a combination of iron and a dialyzed extract of a suprarenal gland. The physiological action of this preparation expresses itself in its regulation of the metabolism of the cells and its influence on the nucleo-cytoplasmic ratio, mitochondria and oxidation.

Invigorating this preparation by adding to it the molecules of sulphuric Tri-naphthylpara-rosanilin, I have received an extremely powerful catalysis which produced a violent liquefaction in the malignant cells, the action of which was selective.

As material for these tests I have employed mice and rats which were bearers of four kinds of tumors: R. Sarcoma no. 10; R. Sarcoma no. 39; M. no. 180 and F. R. Carcinoma. These animals, stock of the Institute for Cancer Research of Columbia University were numbered and already bearers of different kinds of tumors (from 1 sq. cm. to 10×5 cm.). The animals adapted themselves very easily to the injections. Altogether, I have performed about 1000 experiments.

The process of liquefaction began very rapidly; in small tumors sclerosis set in within about 3 to 5 days. Larger tumors dissolved slowly, within about 15 days. In the majority of this series, the percentage of positive cases (the disappearance of tumors) reached 100. In other series, some percentage (about 20 per cent) of mortality was obtained, owing to the too rapid liquefaction of the tumors. A decrease in dose and a repetition of the injection prevent the latter.

In the second series all the experiments made upon six hundred animals yielded identical results, and the animals of this series have now been alive as long as four and five months after cure.

The process of liquefaction begins a few hours after the injection of Corferrol—into the neoplastic tissue. Cytologically, the first phenomenon observed is the decomposition of the mitochondria, the weaker staining of the nuclei, the vacuoles and the cytoplasm between the cells. Following this, the vacuoles enlarge, the tumor cells are transformed into a syncytium and tend to be replaced by vacuoles which promptly move from the center to the periphery of the tumor. These vacuoles cannot be stained by the Best method, nor by osmic acid. The Feulgen reaction is also negative. Eventually the entire tumor becomes filled with these vacuoles which in time are replaced by cicatricial tissue.

During the first few days after injection sections show increased pigmentation in the zona reticularis of the cortex of the suprarenal gland. Three or four days later the cortex of the adrenal returns to normal, and gradually the zona X, which I observed in the tumor bearing animals, disappears. In those animals in which complete liquefaction of the tumor took place, microscopic examination of the cortex presented no abnormalities at the time that the animals were pronounced cured.

It is of interest to note that a change in the hydrogen ion concentration of the tumor tissue takes place as a result of the injection of Corferrol-Pyrrol blue. Whereas an emulsion of uninjected tumor tissue has a pH of 6.7-7.0, that of the injected tissue becomes slightly acid, having a pH of 5.1-5.3.

SOLLMANN, TORALD, H. N. COLE, N. E. SCHREIBER, J. E. RAUSCHKOLB and J. A. GAMMEL (CLEVELAND). **The Clinical Excretion of Mercury.**

This was studied for a variety of mercurial preparations, with different methods of administration. At one extreme are the inunctions and oral administration, for which the excretion is practically continuous, increasing progressively with the administration. The daily urinary excretion reaches the median level of about 1 mgm. for the inunction and 1.36 mgm. for the oral administration at the end of the treatment of 3 to 5 weeks. The median fecal excretion with the inunction method is about one-half of the urinary excretion. This represents the establishment of progressively larger depots of absorption in the skin and intestine respectively.

At the other extreme are the intravenous and intramuscular injections of Novarsurol and Salyrgan. With these the urinary excretion reaches a high level during the first day:

	DOSAGE	URINARY EXCRETION ON FIRST DAY AFTER INJECTION	
		Median	Extremes
	mgm. Hg	mgm. Hg	mgm. Hg
Intramuscular Novasurol.....	33.9	10.5	8.3-12.6
Intravenous Novasurol.....	33.9	12.5	6.5-15.3
Intramuscular Salyrgan.....	37.6	9.6	6.8-15
Intravenous Salyrgan.....	37.6	27	23-36.6

The mercury excretion after the first day, except with the intramuscular Salyrgan, practically ceases, so that at the end of the week the total urinary excretion is:

	DOSAGE	MEDIAN (PER WEEK)	EXTREMES (PER WEEK)
	mgm. Hg	mgm. Hg	mgm. Hg
Intramuscular Novasurol.....	33.9	12	9-15
Intravenous Novasurol.....	33.9	13	7-16
Intramuscular Salyrgan.....	37.6	20	12-25
Intravenous Salyrgan.....	37.6	28	24-38

The fecal mercury excretion is very small (less than 1 mgm.); so that about one-half of the mercury is retained in some immobilized form. There is, therefore, an intensive but very brief excretion of mercury. From the low toxicity, it must be supposed that this mercury acts differently from the ordinary mercury, and is chiefly or wholly in molecular form. Any action which it may have on spirochetes is presumably quite different from that of ordinary mercury.

Other mercurials. The excretion of mercury after intramuscular injection of Binbromide belongs definitely to the first (depot) type.

The excretion of mercury after intramuscular injection of mercury salicylate shows both phases—an acute phase similar to the organic mercurials, followed by a continued and cumulating increase characteristic of the depot type.

Other preparations, including colloidal mercury are being studied and will be included.

SOMOGYI, M. (ST. LOUIS). **An Improved Method for the Preparation of Protein Free Blood Filtrates and the Analysis Thereof.** (Demonstration)

SOSKIN, S. and W. R. CAMPBELL (TORONTO). **The Utilization of Carbohydrate by Totally Depancreatized Dogs, Receiving No Insulin.**

Totally depancreatized dogs, in which the absence of islet tissue was subsequently verified by post-mortem examination, have been maintained without insulin for as long as four weeks. Fed on protein alone, these animals lose weight steadily, but remain bright and active throughout most of the experiment.

For one to two weeks after cessation of insulin administration the animals exhibit an R. Q. of 0.700 or less. The D:N ratio, which starts off at high levels, has frequently fallen below 2.00 by the end of the first week. The ketosis, as judged from urinary excretion, reaches its height about the fourth or fifth day, then steadily declines.

During the remaining *one to three* weeks of the experiment, the R. Q. steadily rises to values as high as 0.900. During this time, the CO₂ combining power and CO₂ content of the blood are not appreciably diminished, and may even rise. The D:N ratio continues to fall, frequently to levels less than 1.00. If insulin be now cautiously resumed, the animal may be revived. It gains weight steadily, and subsequent determinations will again start off with "diabetic" R. Q.'s and D:N ratios.

The addition of fifty grams of glucose to the regular diet, from time to time during the latter half of an experiment, results in the retention of a progressively increasing amount of the administered glucose. The glucose retention, often as much as 60 per cent, is accompanied by a variable effect on the R. Q., and a definite lowering of the urinary nitrogen and ketone excretion.

In view of these results, it would seem advisable to revise some of our present conceptions regarding diabetes and metabolism in general.

SOSNOWSKI, J. (WARSAW). **The Features of the Muscular Twitch.**

The isometric twitch is always—even using the best myographs—accompanied by the shortening of muscle. In order to avoid this shortening completely we can make use of piezoelectric quartz and register the electrical changes with the Cremer-Edelmann string electrometer. The latent period is then easily reduced to the minimum for even the stretching of muscle produced by the local contraction does not interfere with the influence upon quartz. Every change of tension in muscle can be easily and exactly recorded. On the ground of the curves obtained with this method the writer discussed the properties of the twitch under various experimental conditions and in different kinds of muscle.

The methods for recording isotonic twitch and the shape and features of the isotonic curve are discussed.

SPADOLINI, IGINO (SIENA). **Contributo allo studio della fisiologia della milza. Le piastrine e il pigmento ematico nel sangue della vena lienale durante la contrazione della milza. Osservazioni sull'origine delle piastrine in rapporto ai processi di disintegrazione delle cellule endotelioidei negli organi emolinfatici.**

Riprendendo in esame osservazioni personali da vari anni compiute l'A. ha potuto con nuovi esperimenti confermare il fatto da Lui per il primo reso noto fin dal 1924 che la milza costituisce un vero e proprio organo di riserva contrattile per le piastrine del sangue e che la sua contrazione determina l'immissione nel circolo portale di sangue molto ricco in tali formazioni e caratterizzato da un tempo di coagulazione estremamente breve. L'A. ha inoltre dimostrato che nel sangue della vena splenica compare durante la contrazione del viscere una quantità, talvolta notevole, di detrito citoplasmatico e di nuclei liberi più o meno alterati, derivanti in gran parte da elementi a tipo endotelioide. La presenza di questi nuclei o frammenti di nuclei é l'espressione di singolari fenomeni disintegrativi, nucleari e citoplasmatici, che si svolgono attivamente nella milza e nelle ghiandole emolinfatice in genere. A questi fenomeni viene attribuita la maggiore importanza nella formazione dei materiali dai quali traggono la loro costituzione il cromomero e l'ialomero piastrinico.

Dette osservazioni non infirmano l'eventuale provenienza megacariocitica delle piastrine, mettono peraltro in chiaro un meccanismo piastrinogenetico di portata assai più generale. Esso può spiegare molte controversie tuttora esistenti sull'origine di queste formazioni, alla costituzione delle quali concorrono elementi endotelioidi assai più numerosi e diffusi, nelle stesse ghiandole emolinfatice, dei megalocariociti.

In tutto il complesso meccanismo genetico delle piastrine l'A. attribuisce notevole importanza ai fenomeni meccanici che si svolgono nella milza— Negli stessi elementi endotelioidi della polpa splenica si manifesterebbero durante tutto il loro ciclo vitale, sebbene molto limitatamente, processi di disintegrazione nucleare. Il detrito granulare, che viene espulso dai nuclei per un probabile processo di smescolamento dei loro costituenti, dovrebbe venire identificato con le cosiddette "granulazioni azzurrofile" note in molte cellule degli organi ematopoietici.

Indagini compiute sui processi di autolisi del parenchima splenico confermano l'origine nucleare del detrito e delle granulazioni azzurrofile e portano nuovi dati in favore della provenienza citoplasmatica e nucleare rispettivamente dell'ialomero e del cromomero piastrinico.

La distruzione costante di fagociti a tipo endotelioide nella polpa splenica sembra essere una delle cause determinanti la presenza di detrito ematico libero nella milza. Nella contrazione di questo viscere e nell'espulsione del detrito che esso raccoglie é stato identificato il meccanismo con cui si effettua il trasporto al fegato della maggior parte del materiale nucleare ed emoglobinico che continuamente si accumula nella milza in seguito alla distruzione fisiologica degli elementi figurati del sangue e delle cellule proprie dell'organo.

SPIRT, J. (ODESSA). Zur Physiologie und Pathologie des Coronarkreislaufs des Herzens.

Das Problem des Studiums des Coronarkreislaufs des Herzens hat erst in allerletzter Zeit seine Lösung gefunden bei Anwendung des Herz-Lungenpräparats von *Starling* mit gleichzeitiger Einführung in den Sinus coronarius der Tamponkanüle von *Morawitz*. In den Arbeiten von *Starling* und dessen Schule kann eine ganze Reihe mit der Klärung des Mechanismus des Coronarkreislaufs verknüpfter Fragen als erledigt angesehen

werden. Als am meisten umstritten erscheint die Frage nach der Rolle chemischer Faktoren bei dem Coronarkreislauf. Auf Grund unserer Versuche an Herz-Lungen Präparat (Hund) mit gleichzeitiger Einführung der Morawitz-Kanüle und auf Grund von Versuchen an ganzen Tieren (Hunden) unter Anwendung derselben Kanüle kamen wir zu nachstehenden Schlüssen:

1. Die Grösse des Coronarkreislaufs hängt sowohl vom Sauerstoff als auch vom Kohlensäuregehalt im Blute ab.

2. Die Vermehrung des Coronarkreislaufs unter dem Einfluss gesteigerten CO_2 -Gehalt im Blute ist sehr bedeutend und wird nicht immer von Herzdilatation—wie man anzunehmen pflegt—begleitet.

3. Durch unmittelbare Einführung von Kohlensäure ins Blut lässt sich der Coronarkreislauf um das 2-3 fache vermehren (gemeinsam mit Dr. Sribner.)

Zur Klärung der Bedeutung einzelner Aeste der A. coronaria dextra et sinistra für den Coronarkreislauf und die Herzarbeit verwendeten wir, als erste, die Unterbindung dieser Gefässe bei besagter Methodik.

Die Ergebnisse unserer 52 Versuche berechtigen zu nachstehenden Schlussfolgerungen:

4. Die Ligatur einzelner Aeste sowohl der linken als auch der rechten Coronaria führt nur in dem Falle, wenn das Herz im Unterbindungsaugenblicke funktionell stark ist, keinerlei Veränderungen der Grösse des Coronarkreislaufes und der Herzarbeit herbei. Sind aber Zeichen von Herzschwäche vorhanden, so hat die Unterbindung derselben Arterien jäh Verminderung des Coronarkreislaufes mit nachfolgendem des ganzen Herzens.

5. Die Unterbindung beliebiger zwei Aeste der linken Kranzarterie oder des einen derselben mit gleichzeitiger Ligatur der rechten Coronaria bewirkt die gleichen Folgen, die bei Herzschwäche beobachtet werden.

6. Bei einzelnen Versuchen ergibt die Unterbindung der rechten Kranzarterie gewisse Eigentümlichkeiten in der Grösse des Coronarkreislaufes, in dem Sinken des arteriellen und Erhöhung des venösen Druckes und desgleichen in der Veränderung des Herzens selbst.

7. Alle von uns an Präparaten ausgeführten Unterbindungen der Kranzgefässe des Herzens wurden an denselben Gefässen bei ganzen Hunden unter intravenöser Einführung von Germanin "205" wiederholt.

STADIE, WILLIAM C. and F. WILLIAM SUNDERMAN (PHILADELPHIA).

The Osmotic Activity Coefficients of Ions in Hemoglobin Solutions.

The osmotic activity coefficient of an ion is

$$f_i = \frac{\pi}{\pi_0}$$

where π = observed osmotic pressure which can be calculated from Δ the freezing point depression of the solution and π_0 = osmotic pressure calculated from the concentration.

We studied 1, solutions of sodium hemoglobinate, and 2, solutions of NaCl in presence of hemoglobin. The freezing point depression, ion concentration and hemoglobin concentration of a series of such solutions were determined and the osmotic coefficient calculated.

Conclusions: 1. In solutions of sodium hemoglobinate the osmotic activity coefficient of sodium is 0.81 in dilute solutions ($\text{Na} = 30 \text{ mM.}$) decreasing

as the concentration of Na is increased indicating only a partial ionization or activity of Na ion combined with hemoglobin.

2. NaCl in aqueous solutions of hemoglobin has exactly the same osmotic coefficient as in pure water over a great range of concentration indicating that hemoglobin even in large concentration does not affect this property of the ion of NaCl.

STARKENSTEIN, EMIL (PRAG). Die intermediären und terminalen Produkte des Eisenstoffwechsels.

Unabhängig von der Bedeutung des Eisens für die Hämoglobinsynthese ist seine katalytische Funktion im Organismus. Diese ist abhängig von der Bindung des Eisens und seiner Oxydationsstufe. Daraufhin gerichtete Untersuchungen haben ergeben, daß die Bindung und Oxydationsstufe der verschiedenen Eisenpräparate im Organismus verschiedenartige Veränderungen erfahren: es kommt zur Bildung intermediärer und terminaler Produkte des Eisenstoffwechsels.

Alle Eisenverbindungen gehen schließlich im Organismus in ein gleichartiges Stoffwechsel-Endprodukt über, welches im Darm zur Ausscheidung gelangt. Aus einfachen anorganischen Ferroverbindungen—und nur aus solchen—entsteht im Blute durch Oxydation rasch eine Ferrerverbindung (komplexe Ferri-Eiweiß-Verbindung), die als intermediäres Stoffwechselprodukt lange im Blute kreist und schließlich durch Reduktion zu dem erwähnten Stoffwechselendprodukt umgewandelt wird. In dieser intermediär entstehenden Ferri-Eiweiß-Verbindung ist das Eisen anionisch gebunden und sie unterscheidet sich daher grundsätzlich von dem sogenannten Ferrum albuminatum, welches biologisch unwirksam ist und nur ein durch Schutzkolloide in Lösung gehaltenes Ferrihydroxyd darstellt.

Komplexe Eisenverbindungen mit anionischem Eisen bilden auch die Oxypolycarbonsäuren (Zitronensäure etc.); auch diese sind pharmakologisch wirksam.

Da nur die einfachen Ferrosalze, aus denen im Organismus die erwähnte komplexe Ferriverbindung entsteht, und die komplexen Eisensalze der Oxypolycarbonsäuren pharmakologisch wirksam sind, muß geschlossen werden, daß im Organismus nur anodisch wanderndes Eisen pharmakologisch wirksam, kathodisch wanderndes dagegen unwirksam ist. Der intermediäre Stoffwechsel der einfachen Ferroverbindungen ist jedoch verschieden von dem der komplexen Ferri-Eisenoxypolycarbonsäuren; diese werden nämlich im Organismus rascher abgebaut und zum Teile im Harn ausgeschieden, während die aus den Ferroverbindungen gebildete intermediäre komplexe Ferri-Eiweiß-Verbindung im Körper lange unverändert bleibt.

Diese Entdeckung eines biologisch wichtigen intermediären Produktes des Eisenstoffwechsels, welches bisher nur nach Verabreichung von einfachen anorganischen Ferroverbindungen im Körper gefunden wurde, beweist die Sonderstellung dieser Ferroverbindungen als Quelle des im Organismus biologisch wirksamen Eisens.

STARY, ZDENKO (PRAG). Über den Sauerstoffrest der Proteine.

Die Menge der Aminosäuren, welche sich aus dem Totalhydrolysat der Proteine mit unseren heutigen Methoden gewinnen lässt, beträgt im besten Falle 90 Procent des Proteingewichtes. Nach Abzug von einem Molekül H_2O auf ein Molekül Aminosäure ergibt sich, dass in diesem—besten—

Fälle etwa 75 Procent des Proteinmoleküls aus dem Hydrolysat in Form von Aminosäuren wiederzugewinnen sind. Der Rest ist völlig unbekannt. Seine präparative Aufarbeitung begegnet Schwierigkeiten, deren Überwindung vorderhand nicht zu erwarten ist. Der Vortragende hat daher einen anderen Weg zur Aufklärung dieses unbekannten Eiweissrestes versucht. Die Menge C, H, N, O und S, die in den Radikalen der nach Totalhydrolyse gefundenen Aminosäuren enthalten ist, wurde von der Gesamtmenge dieser Elemente in gleichen Protein abgezogen und auf diese Weise die Elementarzusammensetzung des noch unbekannten Eiweissrestes erhalten. Dieser Eiweissrest ist bei allen Proteinen mit alleiniger Ausnahme der Prolamine wesentlich sauerstoffreicher als das Protein selbst.—Zunächst wurde an das Vorhandensein von Kohlehydraten gedacht. Versuche zum Nachweis grösserer Mengen Kohlehydrat bei denjenigen Proteinen, bei denen der Sauerstoffüberschuss am grössten ist, ergaben ein völlig negatives Resultat. Es musste daher auf die Frage zurückgegriffen werden, ob der gesuchte Sauerstoffträger im Hydrolysat überhaupt noch vorhanden ist, oder aber bei der Hydrolyse zerstört wird.—Zur Beantwortung dieser Frage wurde das Protein mit Salzsäure total hydrolysiert, das Hydrolysat im Vacuum bis zur Gewichtskonstanz getrocknet. Die Elementarzusammensetzung des Rückstandes ergab im Gegensatz zum nativen Protein keinen Sauerstoffüberschuss mehr gegenüber dem Anteil der bekannten Aminosäuren. Der unbekannte Anteil des Hydrolysats ist, was seinen Sauerstoffgehalt betrifft, nur wenig von der Summe der bereits bekannten Aminosäuren verschieden.—Es ergibt sich also, dass ein erheblicher Anteil des Sauerstoffs der Proteine während der Hydrolyse an einen flüchtigen Stoff gebunden wird und nach dem Trocknen im Aminosäuregemisch nicht mehr vorhanden ist. Der Sauerstoffüberschuss kann somit nicht durch das Vorhandensein grösserer Mengen einer der bekannten Oxyaminosäuren oder von Kohlehydraten in dem noch unbekannten Eiweissanteil erklärt werden.—Auch um die Abspaltung von Kohlensäure handelt es sich nicht. Die Kohlensäureproduktion während der Hydrolyse reicht nicht aus um den noch ungedeckten Sauerstoffrest zu erklären. Es wird zu prüfen sein, ob die Eiweisskörper nicht Wasser bzw. seine Bestandteile in grösserer Menge enthalten, als sich dies aus der Summenformel kettenförmiger Aminosäureanhydride ergeben müsste.

STEDMAN, EDGAR (EDINBURGH). Chemical Constitution and Miotic Action.

It has been shown by the author (Biochem. Journ., 1926, xx, 719; 1929, xxiii, 17) that the miotic activity of physostigmine (eserine) is associated with the presence in the molecule of a urethane grouping, and that certain compounds of a simpler nature but containing this phenylcarbamate structure possess, in common with the alkaloid, miotic properties. From the investigations carried out it appears that phenyl esters of either carbamic acid or substituted carbamic acids may possess miotic properties but that greatest activity is usually associated, other conditions being the same, with such esters of methylcarbamic acid. In all the cases examined a basic group has necessarily been present in the molecule and it is probable that this grouping is essential to the activity of the urethanes. In any case it is evident from the results obtained with the isomeric dimethylaminophenyl esters of methylcarbamic acid and with the methyl

urethanes of the isomeric hydroxybenzyl dimethylamines that the nature and position, relative to the urethane grouping, of the basic group is of great influence on the extent of the miotic activity. Results leading to similar conclusions have been obtained with the methyl urethanes of the isomeric α -hydroxyphenylethyldimethylamines. These compounds were examined in the form both of their hydrochlorides and methiodides. Great differences in activity were observed, that of the hydrochloride of the methyl urethane of α -hydroxyphenylethyldimethylamine being the greatest and approaching that of physostigmine itself. On account of its great miotic activity the name *miotine* is suggested for this synthetic urethane. An examination of the pharmacological properties of miotine and of other of the above mentioned urethanes has been commenced by Dr. A. C. White of the Department of Pharmacology of the University of Edinburgh. The results so far obtained are of a provisional nature but indicate that the general properties of these compounds are similar to those of physostigmine.

STEDMAN, ELLEN and EDGAR STEDMAN (EDINBURGH). **The Oxygen Dissociation Curve of the Haemocyanin from the Edible Snail (*Helix Pomatia*).**

The oxygen dissociation curve of the haemocyanin in the undialysed serum of the edible snail (*Helix pomatia*) has not hitherto been determined. Using the Van Slyke apparatus under the conditions previously described by the authors in connection with the oxygen dissociation curves of other haemocyanins, this has now been found to be of an S-shape similar to the curves for haemoglobin and for the haemocyanins of other species, despite the fact that in dialysed solution this haemocyanin yields a dissociation curve which is indistinguishable from a rectangular hyperbola. That the inflexion of the curve is not solely an effect of hydrogen-ion concentration is clear from the fact that, in salt-free solution, the curve is not influenced in a detectable manner by changes in pH. Further, it is not wholly due to the presence of sodium chloride, for, in the presence of this salt in a concentration of M/4, the inflexion is much less pronounced than in the undialysed serum.

STEINHAUS, ARTHUR H. and HUGH A. RICE (CHICAGO). **Studies in the Physiology of Exercise. II. Acid Base Balance of Blood in Exercised Dogs.**

As part of an attempt to study the nature of athletic endurance and the effects of diet and training on endurance we studied the acid base picture of dogs' blood before, during and after a bout of exercise carried to the point of exhaustion. Blood samples drawn under oil from the saphenous vein were centrifuged and the serums analyzed for pH employing the new Hastings H ion bicolorimeter and for total CO₂ in the Van Slyke manometric apparatus.

For exercising we used a motor driven treadmill and swimming. During treadmill exercise dogs' rectal temperatures rise markedly and there is tremendous over-ventilation. In swimming heat loss is favored resulting in smaller temperature rises and less hyperpnea. In order to determine the part played by increased body temperature we overheated the same dog in an air bath without exercising.

Our data teach us the following:

1st. In overheating without exercise there is marked alkalosis and lowering of total CO_2 . Both are related in simple fashion to the increased rectal temperature and over-ventilation.

2nd. Exercise by swimming produces at first an increase in the H ion concentration paralleled by a rise in body temperature and a drop in total CO_2 . As the dog grows quieter and swims with less exertion the pH and CO_2 return to approximately pre-exercise levels *in spite of continued exercise*. The rectal temperature drops a little. Moderate hyperpnea which parallels the more acid state is probably provoked by the anoxemia.

3rd. The blood picture in treadmill running appears to be due to a combination of the factors operative in overheating and swimming with overheating playing the dominant rôle. Exhaustion from indoor treadmill running is then largely "heat exhaustion."

4th. Any attempt to explain the mechanism by which exercise affects other bodily functions must take account of the byproduct heat. Especially is this caution valid in attempts to translate "exercise" findings on the dog into human physiology where better facilities for heat regulation are present.

We wish to acknowledge our obligation to Prof. A. B. Hastings for his valued counsel.

STEINHAUSEN, WILHELM (GREIFSWALD). Über die Cupula terminalis in den Bogengangsampullen des Labyrinthes. (Mit kinematographischer Demonstration)

Mit Hilfe einer besonderen Mikro-Methode (vgl. Pflüger's Arch., ccvii) gelingt es, die Cupula in den Bogengangsampullen lebend-frisch zu präparieren. Dabei zeigte sich, dass die Cupula eine völlig durchsichtige, äusserst leicht bewegliche gallertige Masse darstellt. Bei Strömungen der Endolymph wird sie als Ganzes mitbewegt. Durch Aufbringen von feinsten Fremdkörperteilchen (z.B. Aluminiumteilchen) lässt sie sich bei auffallender Spaltlampenbeleuchtung sichtbar machen und photographieren. Es werden Mikrophotographien und mikrokinematographische Aufnahmen der Cupula in Ruhe und in Bewegung vorgezeigt und es werden die Folgerungen aus den experimentellen Befunden für die Theorie der Bogengangserregung diskutiert.

STERN, L. (MOSCOW). Rôle et fonctionnement des "Barrières Histio-Hématiques" dans les diverses conditions physiologiques et pathologiques.

Les rapports entre le sang d'un côté et les divers tissus et le liquide tissulaire de l'autre sont réglés par des mécanismes spéciaux auxquels nous proposons de donner le nom de *Barrières Histio-Hématiques*. La Barrière Hémato-Encéphalique en présente un cas particulier que nous avons étudié dans nos recherches antérieures. Le substratum anatomique des Barrières Histio-Hématiques est constitué essentiellement par l'endothélium des parois vasculaires capillaires. La différence constatée dans le fonctionnement des diverses Barrières fait supposer l'existence des différences correspondantes d'ordre physiques et physicochimiques dans la constitution de l'endothélium vasculaire des divers organes. C'est à ces différences qu'il faut rapporter au moins en partie ce que l'on désigne habituellement comme "affinité" ou "sélectivité" caractérisant certains organes ou tissus par rapport à une substance déterminée (poison, toxine

bactérienne, etc.) introduite dans la circulation générale. Il en est de même du "locus minoris resistentiae."

En collaboration avec H. L. Rapoport nous avons entrepris l'étude de la nature morphologique ou cytologique ainsi que du mécanisme de fonctionnement de ces Barrières. Les expériences ont été faites sur les divers animaux de laboratoire: chien, chat, lapin, cobaye, rat, souris, grenouille, et axolotl. La méthode employée est essentiellement celle que nous utilisons dans nos recherches sur la Barrière Hémato-Encéphalique. Nous examinons simultanément la résistance de ces Barrières vis-à-vis des colloïdes et des cristalloïdes.

En collaboration avec nos élèves Belkina, Gagarina, Guertchikowa, Lokschina, Chvoles, Romel, Zeitlin, Koreischa, et Petroff nous avons examiné l'influence exercée sur le fonctionnement de ces Barrières par l'ablation des diverses glandes endocrines ainsi que par l'administration de préparations actives de ces organes.

Nous avons en outre étudié l'influence de l'asphyxie, de l'avitaminose, de l'inanition, des changements du pH du sang, de l'empoisonnement chronique par l'alcool et la morphine ainsi que de l'intoxication par certaines toxines bactériennes.

STERN, L. (MOSCOU). L'autorégulation de l'activité respiratoire des tissus animaux.

Les recherches antérieures de Battelli et Stern avaient montré l'existence dans les tissus animaux de deux classes de principes: la *Pnéine* et l'*Antipneumine*. Ces substances auxquelles ces auteurs attribuent un rôle important dans la régulation de l'activité respiratoire des tissus se laissent facilement obtenir par l'extraction aqueuse des tissus broyés pris immédiatement ou quelques heures après la mort de l'animal, à un moment où la respiration principale a déjà disparu.

Au cours des recherches entreprises par nous en collaboration avec D. I. Schatenstein dans le but d'établir la marche et la cause de l'affaiblissement progressif de l'activité respiratoire dans les tissus broyés il a pu être établi que le liquide de suspension ayant servi à la respiration du tissu pendant 15 à 30 minutes renferme une ou plusieurs substances pouvant exercer une action nettement inhibitrice sur les échanges gazeux. Cette substance qui agit à la manière de l'antipneumine s'en distingue nettement par ses diverses propriétés chimiques et physiques. Elle représente un des produits de l'activité tissulaire et rentre ainsi dans la grande classe des Métabolites qui règlent les diverses activités des organes et tissus. Elle sert en premier lieu à l'autorégulation de l'activité respiratoire d'un organe donné.

STERN, LINA (MOSCOU). Rôle et fonctionnement des "Barrières Hématiques" dans les diverses conditions physiologiques et pathologiques. (Démonstration)

STEVENS, H. C. and J. M. ROGOFF (CLEVELAND). Some Effects of enervation on Muscular Contraction.

Simultaneous records were made of the contraction of the two gastrocnemii of the frog, in one of which the sciatic nerve was previously severed (at intervals of 7 to 21 days). Certain constant differences in response of the innervated and denervated muscles were observed. The

denervated muscle showed a slight degree of contracture; quicker relaxation; a slower response to the stimulus; and slight tendency to staircase. The bearing of these observations upon the mechanics of muscular contraction is discussed.

STEVENS, H. C., E. KARRER and J. M. ROGOFF (CLEVELAND). **Apparatus for Measuring Muscular Tension. (Demonstration)**

STOLAND, O. O., N. P. SHERWOOD and R. A. WOODBURY (LAWRENCE, KANSAS). **Vagus Chronaxie in Dogs Sensitized to Horse Serum and Modification of Anaphylactic Reaction Following Vagus Faradization.**

The rheobase and chronaxie of the vagus nerve was determined using eighty-two stimuli per second during a stimulation period of two seconds. The chronaxie in a series of twenty-one dogs sensitized to horse serum varied from 0.055 to 0.1156 σ , average 0.0679 σ , while in a series of seventeen normal dogs the chronaxie varied from 0.06 to 0.42 σ , average 0.139 σ . The chronaxie was not changed during the anaphylactic response following the injection of horse serum after blood pressure had returned to approximately normal level.

As a result of the vagus stimulation incident upon determining rheobase and chronaxie the anaphylactic reaction to a test injection of horse serum was found to be modified. In ten sensitized dogs in which the horse serum was injected without previous vagus stimulation the blood pressure fell markedly in 30 to 40 seconds following the injection and the clotting time of the blood markedly increased except in one. In eighteen sensitized dogs the test injection of horse serum was given following stimulation of the vagus. Only six of eighteen gave a typical fall in blood pressure and in only two of the six was the coagulation time increased. In five dogs the fall in blood pressure was atypical in that the onset was delayed and the fall gradual. In only one of the four was the coagulation time increased. Eight sensitized dogs showed no fall in blood pressure and no delay in coagulation time upon injection of horse serum following vagus stimulation.

Our results warrant the conclusion 1, that sensitizing doses of horse serum lead to reduction of chronaxie of the vagus nerve; 2, that the stimulation of the vagus nerve leads to modification of the anaphylactic reaction.

STRUGHOLD, H. (WÜRZBURG). **Der Direkteffekt von temporärer Anoxaemie auf die systolische und diastolische Herzgrösse bei konstantem Rhythmus (Kinematographische Registrier-Methode).**

Wenn diastolischer Arteriendruck, Venendruck und Herzrhythmus konstant gehalten werden, so sind Veränderungen in der Herzgrösse bei temporärer Anoxaemie nur zu erklären durch direkte Einwirkung auf das Herz selbst (Direkteffekt).

Diese Frage, ob wir einen Direkteffekt der Anoxaemie auf das Herz anzunehmen haben, habe ich in einer Reihe von Versuchen an Hunden geprüft. Der Aortendruck wurde registriert mit dem Wiggerschen optischen Manometer, die Herzgrösse mittels kinematographischer Aufnahme des in einer Herzwiege offen liegenden Herzens. Die Beatmung des Tieres geschah durch Einpumpung von Luft mit normalem und solcher mit 12 bis 5 procentigem Sauerstoffgehalt aus einem Tank.

Herzaufnahmen wurden gemacht mit einer Cameraentfernung von 1

Fuss und mit einer Frequenz von 30 pro sec. Die einzelnen Bilder wurden auf einen Schirm projiziert, die Umrisse gezeichnet und die Flächen mittels Planimeter ausgemessen. Bei Beobachtung gewisser Cautelen (z.B. Aufnahme in immer gleicher Respirationslage des Thorax) zeigt diese kinematographische Registriermethode der Herzgrößen unter den hier gegebenen Bedingungen einen Fehler, der nur in ungünstigsten Fällen 8 Procent erreicht. Sie ist exakt genug, um bei der kurvatorischen Darstellung der aufeinanderfolgenden Bilder während eines Herzschlages eine Kurve zu zeigen, die in allen wesentlichen Einzelheiten der Volumkurve entspricht

Ergebnisse. Bei gleichbleibendem Herzrhythmus, Venendruck und Diastol. Arteriendruck stieg unter der Wirkung von *Anoxaemie*, der Pulsdruck u.a. in einem Versuch (nach Einatmung von 45 l. 10.5 Procent O_2 -haltiger Luft) von 22.5 auf 25.5, in einem anderen (nach 15 l. 10.0 Procent O_2 -haltiger Luft) von 17 auf 32 mm. Hg. Ein anderer Hund zeigte nach 13 l. 5.3 Procent O_2 -haltiger. Luft einen Anstieg des Pulsdruckes von 35 auf 60 mm. Hg. In all den Fällen, in denen der Pulsdruck merklich anstieg, wurde die diastolische Herzgrösse erheblich grösser, die systolische in geringerem Masse, (Zunahme des Herzschlagvolumens). Die Austreibungszeit war jedoch nicht, wie man bei der Vergrößerung der diastol. Herzgrösse annehmen sollte, verlängert, sondern verkürzt oder sie blieb dieselbe.

Temporäre Anoxaemie übt demnach einen *stimulierenden Einfluss* auf das Herz selbst aus.

SULLIVAN, M. X. (WASHINGTON). **The Cystine Content of Foodstuffs, Tissue and Urine.**

In continuation of a study of the highly distinctive β -naphthoquinone test for cysteine (or cystine after reduction) described in Public Health Reports, xli, 1030, 1926, it was found that this test requires three free groups SH, NH_2 , and COOH—a condition that explains its remarkable specificity. By attention to certain details, such as the need of more alkali in the reaction to take care of the buffering power of the hydrolysate (Journ. Biol. Chem., 1927, lxxiv, xiv) and by getting concentrated tissue extracts, it was found possible to apply the method to the quantitative determination of cystine in protein, tissue, and urine. Some thirty proteins have been examined and comparison has been made on the hydrolysate with the Sullivan, the Okuda iodometric method, and the Folin-Looney method. The Sullivan method gives lower results but they are in general fairly closely paralleled by the results with the Okuda method. The Folin-Looney procedure gives higher values and so does the Van Slyke procedure, as gathered from the literature pertaining to the same proteins. The lower values, as found by the Sullivan method, are in certain cases verified by the finding of feeding experiments. In tissue work it was found that in certain tissues, cysteine apparently occurs as well as reduced glutathione. On applying the Sullivan, the Okuda, and the Folin-Looney cystine methods to urine a new and highly important discovery was made as to the presence of cystine in normal urine and its states of combination.

SULZE, W. (LEIPZIG). **Über Resorptionsgeschwindigkeit.**

Bei Batrachiern, die in hypotonischen wässrigen Lösungen von Salzen und Anektrolyten gehalten wurden, hat der Vortragende folgende ein-

fache Beziehung zwischen der Konzentration des Bades und der Konzentration des von den Tieren abgeschiedenen Harnes feststellen können: die Badkonzentration, ausgedrückt in molaren Mengen (also Mole Wasser pro Mole Gelöstes) stimmt überein mit der in absoluten Gewichtsmengen (also Gramme Wasser pro Gramme Gelöstes) ausgedrückten Konzentration des Harnes. Diese Gesetzmässigkeit führt zu dem Schluss, dass die Geschwindigkeit der Resorption der einzelnen Molekülararten (sowohl der Moleküle des Wassers als des Gelösten) direkt proportional ist der räumlichen Konzentration (Zahl der Moleküle in der Raumeinheit des Bades) und *umgekehrt* proportional der Masse des einzelnen Moleküls. Es wird gezeigt, wie sich diese Gesetzmässigkeit auch bei der Darmresorption geltend macht (Versuche am Dickdarm des Hundes).

SULZER, R. (BASEL). Zum Verhalten des ruhenden Skelettmuskels bei der Dehnung.

Der Muskel ist seit Blix vielfach als viskös-elastisches System aufgefasst worden. Die Dehnungskurve des ruhenden Muskels widerspricht dieser Auffassung. Bei unendlich langsamer Zustandsänderung eines viskös-elastischen Systems fallen im Längen-Spannungskoordinatensystem die Kurven der Dehnung und der Entdehnung mit der Längen-Spannungskurve seiner elastischen Phase zusammen. Bei Vornahme zyklischer Spannungsänderungen von endlicher Geschwindigkeit liegen die Maxima und Minima der Länge auf der Längenspannungskurve der elastischen Phase. Beides trifft für den Muskel nicht zu; insbesondere ist noch ein Arbeitsverlust vorhanden, trotzdem sich der Muskel bei sehr langsamen Spannungsänderungen praktisch im Gleichgewicht befindet. Diese Tatsache bedeutet, dass sich der Muskel im allgemeinen wie ein unvollkommen elastischer Körper verhält. Die elastische Unvollkommenheit ist in frisch exzidiertem Zustande des Muskels immer vorhanden, sie ist umso grösser, je stärker der Verkürzungsrückstand bzw. die Kontraktur ausgebildet ist, nimmt aber mit steigender Beanspruchung ab und kann wiederhergestellt werden (z. B. durch Reizung, Azetylcholin usw.)

Das Verhalten des Muskels bei unendlich langsamer Zustandsänderung lässt sich gut durch folgendes Modell wiedergeben. Man denke sich einen elastischen Körper, etwa eine Spiralfeder, der Länge nach in eine grosse Anzahl gleichlanger Segmente eingeteilt und jedes dieser Segmente durch einen undehnbaren aber zerreislichen Faden überbrückt, sodass sich das Federsegment nicht verlängern kann, solange der Faden intakt ist. Weiter sollen die Zerreisfestigkeiten der einzelnen Sperrfäden eine Streuung um einen Mittelwert aufweisen entsprechend der Gauss'schen Fehlerfunktion, sodass sie bei steigender Spannung sukzessive durchreissen. Ein solches System weist wie der Muskel auch bei unendlich langsamer Dehnung einen einmaligen Arbeitsverlust auf, verhält sich also zu Beginn ähnlich einem unvollkommen elastischen Körper, nähert sich aber mit steigender Belastung mehr und mehr einem vollkommen elastischen. Ausserdehn erhält man bei geeigneter Wahl der Elastizität und der Konstanten der Gauss'schen Fehlerfunktion im wesentlichen dieselben Kurvenform wie sie der Muskel bei der Dehnung aufweist.

SURE, BARNETT and MARGARET ELIZABETH SMITH (FAYETTEVILLE).

**The Effect of Vitamin Deficiencies on Carbohydrate Metabolism.
II. True Blood Sugar and Alkaline Reserve in Uncomplicated Vitamin B Deficiency of Growing and Adult Albino Rats.**

No disturbance is apparent in the concentration of true blood sugar in uncomplicated vitamin B deficiency of growing and adult albino rats until the terminal stages when an inanition hypoglycemia becomes evident. There is considerable disturbance, however, in the apparent blood sugar due to increases of reducing non-sugar substances, in some cases rising to as high a figure as 80 to 90 mgm. per cent. The average concentration of reducing non-sugars of the control animals was 29 mgm. per cent.

The carbon dioxide volume per cent in plasma of the control animals was found to range from 40 to 60 per cent. In the polyneuritic animals an acidosis was encountered only in the advanced stages of the avitaminosis associated with marked inanition, the figures ranging from 25 to 35 carbon dioxide volume per cent.

SYLLABA, G. (PRAGUE). **The Influence of Saccharin on the Respiratory Exchange and on the Blood-Sugar Level—an Example of the Conditioned Reflex?**

The effect of saccharin on the respiratory exchange and on the blood-sugar curve has been studied. A significant rise in the oxygen consumption and in the blood-sugar level has been observed when saccharin was taken per oz. This increase in the blood-sugar and basal metabolic rate after saccharin seems to be caused partly by a reflex which is involved by the ingested saccharin in the small intestine, partly by a psychical reaction depending on the sweet taste of saccharin.

SZAKÁLL, A. (BUDAPEST). **Die Änderungen der Grundumsatzwerte bei Schwerarbeitern.**

Durch frühere Untersuchungen wurde festgestellt, dass die landwirtschaftlichen Arbeiter in die Gruppe der Schwerarbeiter gehören. Während der Erntesaison beträgt der täglich Energieumsatz 6000 Kalorien. Wir stellten auch fest, dass während dieser relativ kurzen, drei Wochen dauernden Arbeitsperiode die Arbeiter, mit geringer Ausnahme, einen Gewichtsverlust von 5,7 Procent aufweisen. Da diese Gewichtsabnahme sehr rasch zustande kommt und infolge eines Ernährungsdefizits auftritt (die täglich eingeführte Kalorienzahl beträgt ungefähr 4000 Kalorien.), schien es uns vom physiologischen Gesichtspunkte aus wichtig den Grundumsatz dieser Arbeiter einer Prüfung zu unterwerfen.

Wir durchführten mit der Douglas'schen Sackmethode an 4 Arbeitern Grundumsatzbestimmungen während und nach der Erntesaison. Von diesen diente eine Versuchsperson als Controllperson, bei welcher der Energiebedarf mit den täglich eingeführten 6000 Kalorien von Tag zu Tag gedeckt wurde. Die anderen 3 Versuchspersonen genossen freigewählte Kost. Der G. U. wurde jedesmal nüchtern bestimmt.

Bei der Deckung des Energiebedarfes, also bei der Controllperson, fanden wir ein G. U.-Gleichgewicht, d. h. die tägliche Schwankungen waren nicht grösser als 5 Procent. Die G. U.-Werte während der Erntesaison zeigten im Vergleich zu den Werten der nachfolgenden Ruheperiode eine Zunahme von 7.4 Procent. Die respiratorischen Quotienten (R.Q.) schwankten in beiden Perioden zwischen 0,80–0,86.

Bei jenen Versuchspersonen aber, die an freigewählter Kost lebten, konnten in beiden Perioden verschieden grosse Schwankungen in den G. U. wie auch in den R.Q. Werten beobachtet werden. In der Ruheperiode stieg der R.Q. nicht selten über 1.0, blieb dagegen in der Arbeitsperiode unter 0.70, welcher Umstand mit Stoffumwandlungen zu erklären wäre, in sofern während der Arbeitsperiode die Kohlehydratreserven erschöpft werden und Fett verbrannt wird, in der Nachperiode aber Fett aus Kohlehydraten entsteht.

Diese Schwankungen kommen bei der Wertung der Arbeitphysiologischen Versuchsergebnisse in Betracht und es können aus denselben auch auf die inneren Stoff- und Energieumwandlungen und die Erholungs-Erscheinungen Schlüsse gezogen werden.

SZENT-GYÖRGYI, ALBERT (CAMBRIDGE). On the Chemistry of the Adrenal Cortex.

The adrenal cortex contains a highly reducing substance, which is specific for the interrenal system and has been isolated as crystals. It is a hitherto unknown isomer of glycuronic acid. The substance is capable of acting as a powerful catalyst of certain biological oxidations and under certain conditions inhibits pigment formation in minute quantities (1:0,000,025).

An identical substance has been isolated from peroxidase-plants. Here the substance is clearly connected as catalyst with the peroxidase system.

Some chemical properties of the substance are demonstrated.

SZENT-GYÖRGYI, A. and A. N. DRURY (CAMBRIDGE, ENGLAND). On the Action of Adenine Compounds on the Heart. (Demonstration)

An adenine nucleotide has been isolated from the heart muscle, which has, if injected intravenously, a definite action on the heart. The part of the molecule responsible for this action is the adenosine compound. The chemical nature of the substance and its physiological actions are discussed.

TAINTER, M. L. (SAN FRANCISCO). Use of the Cocainized Organism as a Biological Method of Determining the Sympathicotropic and Musclopertropic Actions of Pressor Drugs.

The method consists in comparing the rises of blood pressure obtained with the pressor drugs before and after otherwise ineffective doses of cocaine (10 to 30 mgm. per kilo), injected subcutaneously in cats, dogs or rabbits. In the cocainized organism the pressor response to sympathicotropic drugs (epinephrin) is increased (sensitized), and that to musclopertropic drugs (ephedrine, tyramine, phenylethanolamine, and barium) is either unaltered, abolished or diminished, (desensitized). The results with the pressor drugs tested in the cocainized organism generally corroborate those with the same drugs in the ergotized (or ergotoxinized) organism. Thus, the usefulness of the cocainized organism as a biological method of determining the mechanism of pressor action of drugs is indicated.

TAIT, JOHN and W. J. McNALLY (MONTREAL). A Method of Recording the Responses of Individual Muscles to Appropriate Stimulation of the Semicircular Canals. (Demonstration)

In order to study the response of individual muscles of the hind limbs of

frogs to stimulation of their semicircular canals, a decerebrate frog is divided into two components, a leg component and a head-body component, connected simply by the sciatic nerve. The leg (or, as the case may be, both legs), with muscles connected to appropriate levers, may thus remain stationary in position during such time as the head-body component is being subjected to angular displacements on an adjoining tilt-table.

When a head-body component with both labyrinths intact is suddenly tipped backward, the muscles that flex the ankle-joint exhibit a brief twitchlike contraction. These "twitches," which remind one of tendon-jerks, can be readily and regularly graded in amplitude according to the degree of angular acceleration imparted to the head-body component. The shortest recorded reaction time of the response is 35 σ . With higher angular acceleration of the head-body component the gastrocnemius muscles may exhibit similar twitchlike contractions simultaneously with those of the flexors. Under the special conditions of the experiment, no muscular contraction occurs in the leg component in response to any slowly effected change of position of the head-body component, no matter how extensive; in other words, static reactions are wholly absent.

If the head-body component has been previously delabyrinthised, the muscular responses to angular acceleration are absent. If a labyrinth is removed on one side only, the flexor muscles on the intact side respond best, but the flexors on the opposite side also respond. A similar finding is made when all three canals on one side have been destroyed. Destruction of all six canals, with preservation of the two utricular maculae, abolishes the muscular reaction to angular acceleration.

TALBERT, G. A., ALDEN SQUIRES and FRANK KILGARD (GRAND FORKS, NORTH DAKOTA). **Changes in CO₂ Combining Power of Blood as Affected by Profuse Sweating.**

As a control measure there was first withdrawn from the basilic vein a sample of blood for the determination of the CO₂ combining power by the well-known Van Slyke apparatus for gas analysis. The subject then donned a rubber jacket which enveloped the torso including the arms, after which he was seated in a sweat cabinet where he remained from 45 minutes to an hour or until there was profuse sweating. After retiring from the cabinet another sample of blood was taken in a similar way and a like analysis was made as before. We are able to report 97 determinations in which we find a decrease in CO₂ combining power in 80 instances.

TANGL, HARALD (BUDAPEST). **Die Wirkung einiger Hormone und ultravioletter Bestrahlung auf die Farbstoffausscheidung aus dem Blute.**

Die Ausscheidung der in die Blutbahn injizierten Stoffe erfolgt verschiedenen schnell und hängt zunächst von ihrer kristalloiden und kolloidalen Natur ab. Bei dem Auswandern der Farbstoffe spielt ausserdem noch die chemische Struktur der Stoffe, der Wärme, der Dispersionsgrad eine Rolle. Die Zellen, welche die injizierten Farbstoffe auffallend gut absorbieren, werden im Retikuloendothelialen-System zusammengefasst. In dieses System gehören die Zellen der Lymphknoten, Milz, Knochenmark, Leber und Nebennieren. Besonders grosse Rolle spielt nach meinen Versuchen die Milz, nach deren Herausnahme der Farbstoff viel langsamer ausscheidet als beim Normaltier. Da aber die Milz, nach vielen Arbeitsergebnissen, eine inkretorische Wirkung hat, untersuchte ich die Wirkung der

Milzextrakte auf die Farbstoffausscheidung bei normalen und milzlosen Hunden und fand, dass bei entmilzten Hunden nach Verabreichung des Extraktes der Farbstoff fast so schnell ausgetrieben wird als bei milzhaltigen Hunden. Das beweist, dass die Milz ausser ihren Zellen auch einen hormonalen Stoff entsendet, wodurch der Farbstoff in viel kürzerer Zeit die Blutbahn verlässt. Es ist aber nicht nur das Inkret der Milz, welches einen Einfluss auf das Auswandern des Farbstoffes ausübt, sondern auch der Extrakt der Thyreoidea, der Hypophyse und der Hoden. Die Wirkung besteht darin, dass der Farbstoff unter Einwirkung der Extrastoffe viel langsamer ausgeschieden wird. Farbstoffausscheidung ist auch von der vasomotorisch wirkenden Eigenschaft der Stoffe abhängig; das wird durch Versuche bewiesen, die ich mit Cholin und Histamin ausführte, indem nach Cholingaben die Farbstoffauswanderung schneller, nach Histamingaben langsamer erfolgt. Dies führte mich auf den Gedanken, die Wirkung der ultravioletten Strahlen auch zu untersuchen, da die Strahlung auch auf die nicht bestrahlten Gefässgebiete und auf die Blutzusammensetzung eine Wirkung ausübt. Nach Bestrahlung verschwindet der Farbstoff viel langsamer aus dem Blute, namentlich ist das Verschwinden in der ersten Zeit stark verlangsamt. Bei entmilzten Hunden zeigt sich kein Unterschied nach dem Bestrahlen, dadurch wird es bewiesen, dass durch die Entmilzung die maximale Farbstoffausscheidung erreicht wurde.

TASHIRO, SHIRO (CINCINNATI). Nature and Amount of Bile Salts in Normal Blood.

It is known that the alcoholic extract of blood gives a Pettenkoffer color which is exactly like that obtained with bile salts. The blood substance that gives this color is precipitable by Mg salts in a slightly alkaline medium, suggesting that it is not a cholic acid derivative. If it were a bile salt, it would probably be desoxycholic salts. The colored product of the Pettenkoffer reaction can be precipitated with a Ba salt, and redissolved in 66 per cent H_2SO_4 . The comparison of the colors thus produced by the blood substance, free and conjugated cholic acid, and free desoxycholic acid show that they are alike; but they fluoresce quite differently when subjected to ultraviolet ray using a source of monochromatic light (3660 A. U.). The fluorescent colors thus produced by the blood substance and desoxycholic acid are identical, but that of free or conjugated cholic acid is quite different. If the normal blood contains a bile salt, it is not then a cholic acid derivative, but is probably a derivative of desoxycholic acid. The amount of the substance is about 0.08-0.1 per cent for human blood if calculated as a bile salt, being higher for the dog and lower for the horse.

Could this be a bile salt? If the calculated amount of the total alcohol-acetone extract of the blood be injected into a guinea pig, it does not produce gastric ulcer and death, but when freed from certain lipins, it does produce a gastric ulcer and death typical of that produced by pure bile salts. Since, except all bile salts, the alcohol soluble compounds that are known to produce the Pettenkoffer color do not produce gastric ulcer, but instead antagonize this particular action of the bile salt, the conclusion seems obvious that normal blood, since it contains a substance causing gastric ulcer, contains a bile salt, and it is probably desoxycholic acid. And unless an accelerator be in the blood, the amount of the bile salt in

the normal blood of all animals must be very large, the majority of the colors we produce being due to desoxycholic acid. This large amount of toxic desoxycholic acid in blood is quite harmless because of the presence of its antagonist, largely phospholipins. Except in rare cases, we have found so far neither cholic acid nor its conjugates even in pathological cases, where we can reasonably expect the presence of bile in the blood.

TAYLOR, N. B. and A. FINE (TORONTO). The Excretion of Calcium through the Intestine in Parathyroidectomized Animals.

The question of calcium excretion through the intestine in tetany has

TABLE 1

Excretion through the small intestine after injection of calcium into normal animals

ANIMAL	WEIGHT	CaCl ₂ INJECTED	SERUM CALCIUM		CALCIUM IN FIRST WASHING AT BEGINNING OF EXPERIMENT	CALCIUM IN SECOND WASHING 6 HOURS LATER
			5 minutes after injection	6 hours after injection		
	grams	mgm.	mgm. per 100 cc.	mgm. per 100 cc.	mgm.	mgm.
Cat 48	2,150	125	21.5	10.4	0	0.54
Cat 51	2,500	150	22.5	10.5	0	0.30
Cat 64	1,880	115	24.8	12.9	0	No Ca
Cat 65	2,550	165	25.4	10.4	0.7	Trace
Cat 70	3,150	210	30.1	12.2	0	1.0

TABLE 2

Excretion of calcium through the small bowel after the injection of calcium into the veins of parathyroidectomized animals

ANIMAL	CALCIUM INJECTED	SERUM CALCIUM		CALCIUM EXCRETED	
		After 5 minutes	After 6 hours	Ca in first washing	Ca in second washing 6 hours later
	mgm.	mgm. per 100 cc.	mgm. per 100 cc.	mgm.	mgm.
Cat 49	120	18.3	11.1	0	4.0
Cat 50	160	22.4	10.4	0	10.6
Cat 53	150	20.6	10.7	0	9.0
Cat 63	155	28.8	12.9	0	5.0
Cat 60	180	26.4	13.1	0	5.0
Cat 56	180	23.5	10.1	0	3.4
Cat 61	200	25.9	15.0	0	9.1

been investigated by several workers (Macallum and Voegtlin, Salvesen, Hastings and McIntosh). In previous experiments however the excreted calcium was estimated in the feces of animals placed upon a diet of constant calcium content.

It seemed to us, since in any event we would not expect the differences in excretion of normal and of parathyroidectomized animals would be large, that methods dependent upon the estimation of the calcium of the feces would possess an error which would obscure the true result. The method used by Stewart and Percival by which a portion of the intestine was washed out until calcium free, appeared more likely to yield accurate results. This method with some modifications was used by us throughout.

The excretions in normal and in parathyroidectomized animals were compared after the injection of 60 mgm. of CaCl_2 per kilo intravenously. The general procedure was as follows. The abdomen was opened and cannulae were tied into the lumen of the bowel immediately below the pylorus and just above the ileocolic sphincter. The bowel was then flushed out with 600 cc. of calcium-free saline until the final 100 cc. contained no trace of calcium. The cannulae were closed by rubber caps, the bowel replaced within the abdomen and the animal allowed to recover from the anesthetic. From three to six hours later the abdomen was re-opened under an anesthetic and the bowel flushed out until the washings were again calcium-free. The total calcium of the washings was again estimated.

The determination of the quantity of calcium in the washings was carried out in the following way. The washings were usually cloudy, and contained shreds of mucus and epithelial debris. These were removed by centrifuging, and the calcium in the clear supernatant fluid was then determined by the Kramer-Tisdall method for serum as modified by Clark and Collip. After the first few experiments it was thought advisable to acidulate the fluid before centrifuging, against the possibility that calcium in an insoluble form, such as the carbonate, was being thrown down with the other solid material. Five cubic centimeters of concentrated hydrochloric acid therefore were added to each 100 cc. of the washings. The yield of calcium however was only slightly increased by this addition. In the normal animals the amount of calcium excreted by the bowel was very small, never more than 1 mgm. and usually much less. In the parathyroidectomized animals the excretion was very much greater. The maximum excretion in the series of operated animals was 10 mgm. and the minimum 3.4 mgm. See tables 1 and 2.

THUNBERG, TORSTEN (LUND). **Citric Acid in Animal Fluids.**

The author has described (Biochem. Zeitschr., 1929, cevi, 109) a new biological method for detection of citric acid in very small quantities.

The necessary reagents are: 1, a quite freshly prepared fluid extract of shelled seeds of *Cucumis sativa* (cucumber), 1 part seeds plus 5 parts 0.87 per cent K_2HPO_4 ; 2, methylene blue solution, 1 part in 30,000 parts water; 3, "Thunberg tubes" and the other apparatus of the "Thunberg technic" (Oppenheimer-Pincussen, Die Methodik d. Fermente, 1928, 1118).

The slow methylene blue decoloration in the system cucumber seed extract-methylene blue is accelerated up to perhaps ten times if citric acid is present. Only hexose-diphosphate has a similar effect, but this substance also accelerates the decoloration in a system of orange seed extract-methylene blue, which citric acid does not do.

The method makes a quantitative determination of citric acid possible, because the least necessary amount of citric acid for giving the maximum acceleration of the decolorisation is easy to determine. For analysis of the citric acid content of an unknown fluid one has only to find out just how much one has to add to get the shortest decoloration time. Less than 10 mikrogramms citric acid can be estimated with the method. It is not necessary to isolate the citric acid in animal fluids for the determination.

A systematic study of the citric acid content of animal fluids is going on in the author's laboratory. Some results follow:

ANIMAL FLUID	CITRIC ACID CONTENT IN PARTS PER THOUSAND	INVESTIGATOR
Urine (citric acid is never absent in urine from healthy people; it may go down to zero in nephritis)	0.25-1.8	Östberg
Women's milk contains no citric acid before two days after delivery. The citric acid content then going up rapidly to	1.5	Jerlov
Cerebrospinal fluid	0.05-0.06	Benni
Fluid from epididymis of rabbit	2.5	Schersten
Fluid from seminal vesicles of rabbit	1.5	Schersten
Fluid from seminal vesicles of pig	6	Schersten
Sperm of man	1.8-4.1	Schersten
Sweat	About 0.1	Schersten
Blood serum of man	Less than determinable	Östberg

TIGERSTEDT, CARL (HELSINGFORS). On the Morphology of the Central and Peripheral Pulse.

By means of the artery in question as a manometer central and peripheral pulse-curves are simultaneously registered. The results of some experiments will be described.

TSCHERMAK, A. (PRAGUE). Weitere Studien über Elektrogastrographie.

Vortr. erinnert zunächst an seine ältere Feststellung, dass die normale Rhythmik des Magens—nach Beobachtungen am Froschmagenring—von bioelektrischen Erregungsströmen begleitet ist, welche früher einsetzen als die Kontraktion, ein—oder zweiphasisch verlaufen und in ihrer Stärke nicht einfach der mechanischen Leistung parallel gehen. Es zeigte sich ferner, dass den normalen Spontankontraktionen einfache oder höchstens doppelte Erregungen zu Grunde liegen, dass also die ersteren als Einzelzuckungen oder höchstens als binäre Superpositionen, nicht als Tetani anzusehen sind. In neueren Versuchen liess sich auch bei exakter Ableitung von der Reizstelle selbst ein sicheres Latenzstadium des bioelektrischen Aktionsstromes von erheblichem Betrage (Zehntel—bis ganze Sekunden) feststellen. Dasselbe ist nach mechanischer Reizung anscheinend kürzer als nach elektrischer, wächst bei Schädigung (Abtrennen der Schleimhaut) und beim Absterben, nimmt hingegen mit der Reizstärke etwas ab. Vortr. fasst dasselbe—ähnlich wie er es am Herzen getan—als den Zeitverlust auf, welchen die Erweiterung der schematisch angenommenen Poren der Zellmembran von der Kationen grössse bis zur Anionen grössse beansprucht. Ferner gelang es durch längerdauernde faradische Reizung als bioelektrische Reaktion Serien von Aktionsströmen und als mechanische Reaktion echten Tetanus hervorzurufen; nach einem solchen zeigen auch die geweckten Spontanreaktionen sowie die effekte mechanischer Reizung für einige Zeit tetanischen Charakter. Am absterbenden Präparat kamen künstlich ausgelöste wie auch spontane Erregungsströme ohne anschliessende Kontraktion zur Beobachtung. Die Magenmuskulatur ist demnach sowohl zu einfacher Zuckungsreaktion wie zu komplexer rhythmisch tetanischer Reaktion befähigt, wird jedoch normaler Weise wesentlich nur zu elementarer Reaktion beansprucht. Hingegen dürften die

pathologischen Magenkrämpfe tetanischen Charakter tragen. Analoges wie von der Magenmuskulatur scheint von Lymphherz zu gelten, während das Blutherz der Vertebraten normalerweise nur mit Zuckung reagiert und der Skelettmuskel zwar auch zu beiderlei Reaktionsweisen befähigt ist, jedoch physiologischer Weise nur tetanisch beansprucht wird und nur beim Sehnenreflex elementar reagiert. Für elektrogastrographische Versuche am unversehrten Säugetier und Menschen hat Votr. eine Sonde konstruiert, welche gestattet einerseits vom Mageninneren mittelst Platinoliven (die eine verschiebbar nach dem Prinzip der Bellocq'schen Röhre) zum Saitengalvanometer abzuleiten, andererseits genau an der einen Ableitungsstelle selbst eine künstliche elektrische Reizung zu setzen und deren Effekt mit dem normalen Elektrogastrogramm zu vergleichen.

Tso, ERNEST (PEPING). A Vegetable Milk Substitute for North China.

A consideration of the scarcity of animal proteins in the food supply of the Orient led to experiments with a vegetable milk substitute for the rearing of infants. The proteins of this "milk" are the soybean proteins. The basic portion is a milk-like fluid obtained by the fine grinding of fresh water-soaked soybeans. This "milk" contains 4.4 per cent protein, 1.8 per cent fat, 1.5 per cent carbohydrate, 0.018 per cent calcium, 0.057 per cent phosphorus and 0.41 per cent total ash. In the diet built upon this basis the proteins constitute 20 to 22 per cent of the calorie intake. Fifty per cent of the total calories are obtained from this "milk," the supplementary food being cane sugar, corn or rice starch, cod liver oil, calcium lactate, sodium chloride and cabbage water, the latter as the chief source of vitamin C. This mixture is well utilized and has proven to be biologically complete. The "milk" alone is comparable to cow's milk in vitamin A and richer in vitamin B, while vitamin C has to be added. Vitamin D is believed to be absent. Without extra additions, the "milk" is inadequate in sodium, chlorine and calcium. Six infants, one from birth and the others a few weeks old, were successfully fed six to nine months on this diet. Their weight curves follow very closely the average weight curve of healthy nursing infants in the United States as well as the average weights of several hundred Chinese breast-fed infants who visited the College Dispensary for minor complaints. Their mental and muscular development and nutritional status in general appear to be as good as what one sees in normal infants reared on milk diets.

Simultaneously with these feeding trials, animal experiments with rats gave similarly satisfactory results. (Growth curves and photographs from infants and rats.)

TULLIO, PIETRO (CAGLIARI). Experiments on Animals. (Demonstration)

TULLIO, PIETRO (CAGLIARI). I riflessi sonori. (Con dimostrazioni cinematografiche)

Praticando un foro nel canale semicircolare osseo del labirinto acustico del piccione, in vicinanza dell'ampolla, ad ogni suono l'animale fa col capo un movimento nel piano del canale, movimento che segue tutte le variazioni di durata e intensità del suono stesso. Forando il canale orizzontale l'animale muove il capo nel piano orizzontale, dirigendolo verso il lato opposto, forando il canale superiore l'animale innalza il capo e lo abbassa se il foro è fatto nel canale posteriore.

Se con la cocaina si paralizza l'attività dell'ampolla corrispondente, il moto s'inverte prevalendo l'attività delle altre due ampolle.

Il movimento riflesso è dovuto a correnti che col suono si formano nel liquido endolabirintico e che battono contro le creste acustiche.

Forando la capsula ossea labirintica in corrispondenza dell'otricolo, l'animale esegue un movimento di rotazione col capo attorno all'asse anteroposteriore, piegandosi il vertice verso il lato opposto, e il moto è accompagnato da deviazione degli occhi. Tale moto si ottiene in grado molto minore anche nel piccione integro, come pure in diversi altri animali e anche nell'uomo, specialmente in casi patologici.

Questi riflessi che accompagna no ogni suono e rumore valgono a localizzare i suoni nello spazio, formano parte integrante del ritmo e della parola, e, differenti per ogni fonema, sono l'origine naturale della scrittura.

TULLIO, P. e O. BUSINCO (CAGLIARI). Le modificazioni della grandezza del cuore nell'asfissia acuta. (Con proiezione cinematografica e diapositive)

Ponendo a nudo il cuore del coniglio ed interrompendo la respirazione artificiale si nota che il viscere, dopo una lieve diminuzione, va incontro ad un aumento della sua grandezza raggiungendo anche quattro volte il volume normale. A seconda che il polmone contenga più o meno aria, il fenomeno compare più o meno rapidamente e si può seguire colla cinematografia. A torace integro il fenomeno si può dimostrare colla radiografia, e poichè la dilatazione impiega 40" a presentarsi, è possibile osservarla anche nell'uomo coll'invitarlo a trattenere il fiato fin che può resistere. La dilatazione interessa le varie cavità del cuore come appare dalle radiografie.

Questa prova può dare utili ragguagli per provare la resistenza dell'apparato circolatorio.

VALLAGNOSC, L., E. HERZFELD et J. GAUTRELET (PARIS). La réserve alcaline après injection d'adrénaline.

Ayant pratiqué la mesure de la réserve alcaline par le procédé volumétrique de Van Slyke, après injection de 1/10 de milligr. d'adrénaline chez le chien chloralosé, nous avons constaté une élévation très marquée de la R.A. (10 à 40%), presque immédiate (1 à 3 minutes après l'injection) mais de courte durée: 5 minutes plus tard la R.A. atteint son taux normal; elle s'abaisse ensuite progressivement: nous avons enregistré une chute de 40% après 2 heures.

Parallèlement à la hausse de R.A., le pH subit en général une hausse passagère, mais nettement marquée (0,7 à 2,3%).

La cause de la tendance à l'alcalose ainsi observée pendant la phase d'hypertension et coïncidant souvent avec une phase d'apnée plus ou moins prolongée a retenu notre attention. Le fait qu'après section des vago-sympathiques l'adrénaline ne provoque plus de modification sensible de la R.A. montre que la hausse de R.A. normalement observée, ne saurait trouver sa cause dans la vasoconstriction générale et pulmonaire ou la dilatation des bronches; l'apnée ne saurait davantage suffire à en rendre compte: nous avons, au cours d'apnées de 1 à 5 minutes provoquées chez le chien par excitation du bout central du vago-sympathique ou par l'hyperventilation préalable, constaté que la R.A. subissait une augmentation légère, très inférieure (2 à 4%) à celle qui coïncidait avec l'apnée adrénalinique.

Etant donné l'augmentation des échanges généralement observée sous l'influence des injections suffisamment lentes d'adrénaline, nous nous demandons si l'augmentation brusque du métabolisme conditionnée par l'intégrité des vasosympathiques est susceptible de rendre compte d'une invasion aussi rapide du courant circulatoire par CO_2 .

Signalons en terminant que l'yohimbine supprime en même temps que la hausse de pression et l'apnée, l'augmentation de la R.A. consécutive à l'injection d'adrénaline.

VAN DYKE, H. B., PERCIVAL BAILEY and PAUL BUCY (CHICAGO). **The Oxytocic Substance of Cerebrospinal Fluid.**

Except for experiments employing the amphibian melanophore reaction, practically all of the convincing evidence for the secretion into the spinal fluid of the active principles of the *pars nervosa* of the hypophysis is based on the detection of an oxytocic substance. All of the previous experiments were performed with uterine bath-fluids entirely unlike cerebrospinal fluid particularly as to pH, and bicarbonate and calcium-ion concentrations. Since van Dyke and Hastings¹ have pointed out the marked changes in uterine response to posterior-lobe extract when carbonate and particularly calcium ion concentrations are altered, the present experiments undertaken for another purpose were performed with uterine bath fluids of the same ionic concentration as cerebrospinal fluid. The data were obtained for the most part with canine cerebrospinal fluids secured by *cisterna* puncture and used in a 90 per cent concentration which is much greater than other workers have employed.

It was early found that if care was exercised in keeping constant the calcium-ion concentrations of the artificial fluid and the cerebrospinal fluid bathing the isolated guinea pig uterus, no oxytocic substance could be found in cerebrospinal fluid. On the other hand if cerebrospinal fluid contained 0.2 to 0.7 mm of calcium per liter more than the bath fluid, there was a marked oxytocic effect. The reduction of the spinal fluid calcium concentration to one equaling that of the artificial bath-fluid involved no destruction of posterior lobe oxytocic substance. Moreover oxytocic responses similar to those provoked by pituitary extract could be readily elicited by artificial "spinal fluid" the calcium-ion concentration of which was greater than that of the bath fluid. Since the artificial isotonic solutions commonly used by others contain from 15 to 30 times as much calcium as is at equilibrium with calcium carbonate, it is believed that the positive or negative results of previous workers depended on the differences or similarities in ionic concentrations (particularly of calcium the *final* concentration of which was unknown) of the artificial solution chosen and the spinal fluid.

VERDA, D. J., F. C. GREEN and W. E. BURGE (URBANA, ILLINOIS).

Evidence that the Phosphorus of the Spermatozoön is in Part Responsible for the Increased Metabolism of the Ovum Following Fertilization.

It is known that the respiratory metabolism of the ovum is increased after fertilization, and that the head of the spermatozoön is rich in phosphorus. The object of this investigation was to determine the effect of the phosphorus of the spermatozoa, as well as the inorganic phosphates, on metabolism or more specifically sugar metabolism.

¹ H. B. van Dyke and A. B. Hastings. Amer. Journ. Physiol., 1928, lxxxiii, 563.

Eight hundred cc. of 0.1 per cent dextrose solution were prepared and divided into portions of 100 cc. each. Each 100 cc. portion was introduced into a beaker and two goldfish of approximately the same size, and with a combined weight of approximately 5 grams, were introduced into each beaker. Air was bubbled slowly through the sugar solutions to insure an adequate supply of oxygen to the fish. One cubic centimeter of fresh sterilized semen was added to one beaker; 50 mgm. of desiccated semen to another; the ash from 50 mgm. of semen to another; the phosphate precipitate from 50 mgm. of semen to another; the filtrate from the phosphate precipitate to another; 50 mgm. of di-sodium phosphate to another; 50 mgm. of di-potassium phosphate to another, and the remaining beaker to which nothing was added served for control. Small portions of the sugar solutions were removed from each of the beakers and sugar determinations were made immediately and after thirty hours, at the end of the experiment, according to the method of Benedict.

The following is the average for six series of experiments. The control fish used 27 per cent of the sugar in 30 hours; the fish to which the fresh sterilized semen was added used 51 per cent; those to which the desiccated semen was added, 55 per cent; those to which the ash of the semen was added, 41 per cent; those to which the phosphate precipitate was added, 41 per cent; those to which the filtrate from the phosphate precipitate was added, 26 per cent; those to which the di-sodium phosphate was added, 53 per cent, and the fish to which the di-potassium was added used 56 per cent of the sugar. Hence it is concluded that the stimulating effect on sugar metabolism of the spermatozoa or semen is due for the most part to the phosphorus content.

VERZÁR, FREDERICK (DEBRECEN, HUNGARY). The Absorption of Fat.

The reaction of the small intestine is slightly acid or neutral. At this reaction the higher fatty acids can not exist in the form of soaps. The supposition that the fats are absorbed in the form of soaps can therefore be omitted. Hence the necessity of a new explanation of fat absorption.—It was shown that both tauro- and glycocholic acids combine in watery emulsions with the higher fatty acids (palmitic, stearic and oleic acids). The resulting combination product dissolves clearly in water, even at pH 6.25 and diffuses without difficulty through parchment membranes. This explains the importance of the bile acids, since in the form of such combinations the fatty acids are absorbed even at the acid reaction of the intestine. The combination of glycocholic and taurocholic acid with fatty acids is molecular; in greater concentrations there exist, however, also greater aggregates. This is shown by measuring those quantities of bile acids which combine with the fatty acids and by the nephelometric analysis of these solutions. Diffusion experiments show that in very diluted solutions nearly all of the fatty acid is diffusible, while in concentrated solutions only a part of it. Through fractionated diffusion it is possible to get out all diffusible fatty acid. Whereas the fatty acids became diffusible, on the other hand the diffusibility of the bile acids decreases. It may be mentioned that fatty acids in finest emulsions do not diffuse at all. Also neutral fats in finest emulsions do not diffuse even if glycocholic acid is present. The polydisperse nature of the fatty acid solutions with glycocholic acid was also shown by ultrafiltration. The stalagmometric analysis of these solutions agrees also with the assumption that

these are real molecular combinations existing in neutral and even in acid solutions (up to pH 6.25). Only this action of glycocholic and taurocholic acid on the fatty acids makes the absorption of fats possible and explains it under physiological conditions.

VERZAR, F. (DEBRECZEN). Diffusion Experiments with Fatty Acids in the Presence of Bile Salts. (Demonstration)

VOEGTLIN, CARL, FLOYD DEEDS, HERBERT KAHLER and SANFORD M. ROSENTHAL (WASHINGTON, D. C.). Simultaneous Measurement in Living Tissues of Electron Equilibrium and Hydrogen-Ion Equilibrium.

Using two improved *static* vacuum tube voltmeters, previously checked against a Compton electrometer, and obtaining photographic records by means of an oscillograph, we have simultaneously and continuously followed the potentials developed at a glass electrode and at a bare platinum electrode. In purely chemical systems the glass electrode specifically records changes in hydrogen-ion equilibrium, whereas the bare platinum electrode measures a "compound" equilibrium composed of hydrogen-ion equilibrium, oxidation-reduction equilibrium, in fact, all electron equilibria.

Under constant conditions resting living muscle *in situ* is characterized by constant values at both electrodes. Changes in conditions induced by a variety of means, such as asphyxia, anaesthesia, cyanide and lactic acid injection, alter the hydrogen-ion equilibrium little if any, while the "compound" electron equilibrium indicated by the platinum electrode shows marked changes. Within certain physiological limits reestablishment of the original conditions results in a return to the former potential values for both electrodes. With these physiological restrictions the potential changes are reversible.

Death is invariably followed by a shift towards positivity at the glass electrode, *i.e.*, increased acidity, while the platinum electrode shifts towards increased negativity, indicating that the increased acidity of the tissue is overshadowed by other electron changes.

VOLBORTH, GEORGE W. (KHARKOV). The Nature of the Inhibitory Process and the Identity of All Kinds of Inhibition in Conditioned Reflexes.

Using Pavlov's method of salivary conditioned reflexes the author establishes the fact that a neutral external stimulus when repeatedly coinciding in time with the process of inhibition in the hemispheres becomes able to provoke the state of inhibition. This has been demonstrated by special experiments for all cases of inhibition of conditioned reflexes internal as well as external. These experiments give evidence that the inhibition in all cases is caused by a special state capable of connecting with any stimulus to form inhibitory conditioned reflexes, just as the state of excitation, when coinciding with a neutral stimulus, brings about a conditioned reflex exciting a certain activity. As one meets in these two cases with two opposite effects (inhibition and excitation) these inhibitory reflexes were termed the negative conditioned reflexes in contrast to the positive conditioned reflexes exciting certain activities. It is of particular interest to emphasize the same nature of the inhibitory process in the cases of external inhibition. In a special series of experiments it has been shown, that a positive conditioned stimulus, the effect

of which has been checked by external inhibition, passes through a period of increasing action, *i.e.*, through the state of positive induction, before returning to the normal level of its action. Up to these experiments the positive induction has been observed only after the process of internal inhibition and its appearance after the external inhibition is a strong support of Pavlov's view, that the process by which the inhibition is brought about is identical in both cases in the internal and external inhibition.

VORONOFF, S. and G. ALEXANDRESCU (PARIS). **Physiological Results of Testicular Grafting in Relation to the Histological Aspect of the Grafts Removed at Intervals During Four and a Half Years Following the Operation.**

Thanks to ten years of observation of a number of grafted animals and men, the successive phenomenal results of the transplantation are now definitely established. They are as follows:—No notable change during the first two months; then a gradual improvement in muscular strength; better appetite; better working of organs hitherto enfeebled; and, in the case of men, greater capacity for intellectual work; lower blood pressure; better metabolism. These symptoms are very marked during the first 2–3 years but fall off gradually until, in the fifth year, they disappear.

Professor Retterer and Dr. G. Alexandrescu have studied the various histological aspects of sections of grafts removed from animals and men in relation to the successive physiological changes. Thirty of these histological sections and ten microscopic photographs shown at the Congress will illustrate the histological changes observed in the grafts from twelve hours after the operation up to four and a half years afterwards.

At first one notices a kind of disorganisation of the tissues. Later one sees a reorganisation of the grafts and the formation of numerous ducts. The histological aspect is no longer that of a normal testicle, but one clearly distinguishes two zones. The peripheral zone, well vascularised, where the seminiferous ducts preserve the epithelial cells in all their vitality: between these ducts one notices the epithelioid cells, the young connective tissue and elements of infiltration. In the centre, however, the histological elements are in a state of hypobiotrophy. Sections removed after two years and two years and a half present the same aspect; but, as time goes on, the fibrous transformation or evolution of the cells becomes more and more evident and after three and a half years the fibrous tissue predominates. In a section removed four and a half years after transplantation, and shown at the Congress, one notices the scarcity of epithelial elements and the transformation of the grafts into fibrous tissue. The physiological results, which may be attributed to the hormonal activity of the grafts, then completely disappear.

WADDELL, J. A. and G. T. GWATHMEY, JR. (CHARLOTTESVILLE, VIRGINIA). **Magnesium Salts per Rectum.**

Experiments were performed in which magnesium salts were administered *per rectum* to rats, rabbits, cats, and guinea pigs. Expulsion was prevented by clamping or ligating the anal canal. Solutions of the various salts were prepared to contain in equal volumes equivalent amounts of magnesium. The concentrations employed were from 8 per cent to 30 per cent in the case of the chloride, or the equivalent where other salts were administered.

The following were readily absorbable: Chloride, acetate, nitrate, ethyl-sulphate, sulphate, and benzoate. The phenomena exhibited were, severally, according to dosage, somnolence, anesthesia, coma, and death (respiratory). The slightly soluble citrate and lactate were ineffective.

Data were secured on the influence of varying 1, the total quantity of magnesium; 2, the concentration of its solutions, and 3, the anion of its salt. The effects of a specific salt were not proportionate to the quantity of magnesium administered. Even a slight change in the strength of a solution markedly altered the response; for instance, 0.1178 gram of magnesium as chloride was in 8 per cent solution ineffective but in 12 per cent anesthetic. The margin of safety between the anesthetic and fatal doses progressively decreased with the concentration. Any statement of dosage is incomplete unless the strength of solution is indicated. The effects of different salts were not proportionate to their content of magnesium. Each required a different total quantity of magnesium and a different optimal concentration; for example, to produce anesthesia, 0.0883 gram of magnesium as benzoate was effective in 9 per cent suspension, but not less than 0.1178 gram as chloride in 12 per cent solution and 0.1478 gram as sulphate in 29 per cent solution. In comparing different salts, consideration must be given not only to the quantity of magnesium but also to the optimal concentration and to the anion.

It was noted further that the efficiency of magnesium was 1, promoted by admixture with certain substances (*e.g.*, sodium benzoate) and by dryness of the feces, and 2, impaired by diarrhea and diuresis.

WAGNER, R. J. and F. M. ALLEN (MORRISTOWN, NEW JERSEY). Gaseous and Carbohydrate Metabolism in Bullfrogs after Removal of the Liver and the Pancreas. (Demonstration)

A method is described to remove pancreas, liver, and small and large intestines by means of saving the small veins of the abdominal wall. These veins carry the venous blood of the posterior extremities and of the kidneys instead of the ligated v. cavae. This gives us a method to study the carbohydrate metabolism after the two main organs for the control of the carbohydrate metabolism are excluded.

1. Frogs after removal of the liver alone survived for 3 to 5 days.
2. Frogs after removal of the pancreas alone survived for about a week.
3. Frogs after removal of liver and pancreas survived for two to three weeks and longer.

The basal metabolism of the total operated frogs is diminished by $\frac{1}{3}$ to $\frac{1}{4}$ of the former value.

Frogs after the total operation do not show any hypoglycemic symptoms, nor any symptoms which could be attributed to accumulation of toxic products of the protein metabolism.

The respiratory quotient of the fasting animal is unchanged. After injection of glucose into the dorsal lymph bag, there is still the elevation of the R.Q. to values near 1. But the increase of carbon dioxide production, indicating the combustion of carbohydrate is retarded. The total CO_2 production, however, is unchanged. Only after repetition of the test 3 or more times there seems to be a negative carbohydrate balance, as also indicated through a higher rise in the blood sugar, if it is permissible to draw any conclusions from a few blood sugar tests.

According to the described experiments, there is the possibility of a

prolongation of the life of hepatectomized animals by means of removal of the pancreas and vice versa. The removal of the pancreas together with the liver inhibits the hypoglycemic shock, which is the main cause of the death of the hepatectomized animals. On the other hand, there is absence of the toxic products of the intermediate metabolism of the liver with their almost unknown influence on the carbohydrate metabolism of depancreatized animals. The removal of the intestine excluded any possible accessory islands and the danger of poisoning the organism with toxic products formed in it.

WALDSCHMID-LEITZ, ERNST (PRAG). Über die proteolytischen Enzyme in tierischen Organen und Geweben.

Das proteolytische System der tierischen Organe und Gewebe, beispielsweise in Milz, Leber, Niere oder Magenschleimhaut, besteht aus einer eigentlichen Protease, zur Hydrolyse von genuinem Eiweiss befähigt, vom Reaktionsoptimum gegenüber Gelatine $\text{pH} = 4-5$, ferner einer Polypeptidase und einer Dipeptidase, deren Angriff auf Peptide und Peptidderivate abhängt von der Natur der chemisch aktiven Gruppen in Nachbarschaft zu der zu spaltenden Peptidbindung, also z.B. von der Anzahl der Aminosäurereste. Dies entspricht den Erfahrungen über die Spezifität und Angriffsweise pflanzlicher Di- und Polypeptidase. Auch die Protease der tierischen Organe, das Kathepsin, ist in ihrer Wirkungsweise pflanzlichen Proteasen, z.B. dem Papain oder der Hefeprotease, verwandt: wie diese reagiert sie mit den isoelektrischen Proteinen und wie diese zeigt sie sich spezifisch aktivierbar durch Blausäure und durch Schwefelwasserstoff, welche im natürlichen Milieu durch einen in den Organen erst bei der beginnenden Autolyse gebildeten Aktivator natürlicher Herkunft ersetzt werden. Durch die Aktivierung wird der Spezifitätsbereich des Kathepsins erweitert: natürliche Proteine werden nämlich nur durch das aktivierte Enzym gespalten, gewisse proteolytische Abbauprodukte dagegen schon durch das aktivatorfreie Kathepsin. Eine Selbstaktivierung des Kathepsins tritt nicht nur bei der Autolyse normaler Organe, sondern auch bei der Bildung und Reifung bösartiger Geschwülste ein; so enthalten reife Tumoren und Sarkome die Protease in aktiviertem Zustand, für den Eiweissumsatz der reifen Tumor- oder Sarkomzelle scheint danach die Gegenwart eines proteolytischen Aktivators kennzeichnend zu sein. Die Aktivierbarkeit der Eiweisspaltung durch Blausäure und durch Schwefelwasserstoff weist ferner auf die Möglichkeit eines Zusammenhangs zwischen den Erscheinungen des gesteigerten Eiweissumsatzes einerseits, der Hemmung der Zellatmung andererseits in den bösartigen Geschwülsten hin; für diese beiden Entartungen des Stoffwechsels könnten auch im Organismus die nämlichen Stoffe verantwortlich sein.

WALTNER, K. (SZEGED). Beiträge zur Kenntnis der Knochenmarkfunktion.

Die Knochenentwicklung ist weitläufig von der Funktion des Markes abhängig. Bosányi hat gezeigt, dass die rachitische Ossifikations-, respektive Kalzifikationsstörung auf eine Dysfunktion des Knochenmarkes zurückzuführen ist. In unseren Untersuchungen zeigte das auf die erythropoetische Tätigkeit des Knochenmarkes sehr intensiv wirkende Eisen in entsprechender Menge gereicht (2 Prozent (der Nahrung) reduziertes Eisen oder die äquivalenten Mengen von Ferrophosphat oder zitronensaurem

Eisen) eine eingreifende Wirkung auf die Knochenentwicklung: bei jungen Versuchstieren (Ratten, Kaninchen) entwickeln sich schwere rachitische, bei älteren Tieren porotische Veränderungen. Magnesiumverfütterung (2 Procent) hat eine Osteoporose und Oligochromämie zur Folge. Bei Kobaltverfütterung entstehen gleichfalls porotische Veränderungen der Knochen und gleichzeitig entwickelt sich eine ausgesprochene Polycythämie und Polychromämie. Bei der Anwendung von 2 Procent Kobalt sind die Blutveränderungen schon nach einer Woche, die Knochenveränderungen nach 2 Wochen sehr ausgesprochen. Diese Untersuchungen zeigen die Einflussbarkeit der Knochenbildung und Blutbildung durch ein und denselben Faktor.

WANG, CHI CHE, BERNICE HUDDLESTON and OTTO SAPHIR (CHICAGO).
The Influence of Protein Level on the Rate of Growth and the Morphology of Organs.

The voluminous literature that has appeared has not as yet given a firm basis for a settlement of the optimum daily protein requirement of growing children. This investigation was, therefore, planned to determine the influence of protein level on the rate of growth and morphology of the organs.

Two series of experiments were conducted on 8 children between the ages of 4 and 12 years. In the first series the children received a diet containing 2 grams of protein and sufficient carbohydrate and fat to make 80 calories per kilo of body weight. The caloric value of the second diet was the same, but the protein was increased to 4 grams per kilo of body weight.

Metabolic studies showed that without exception the rate of growth was more than doubled during the high protein period, the average gain being 82 grams per child per day as against 29 grams for the low protein diet. The rapid growth was accompanied by an increased nitrogen retention averaging 0.084 gram per kilo per day on high protein diet as against 0.039 gram on the low.

As it was impossible to use human subjects for the study of morphology and unwise to carry experiments of this nature for a long period on children, the problem was transferred to rats. Similar investigations have been reported by many investigators, but in no instance was the protein intake calculated according to body weight.

The plan of this investigation was first to use a single protein and later supplement it with amino acids or use a combination of different proteins. In this first series casein was chosen as the sole source of protein and the amount used in the first two diets was similar to that contained in the experiments on children. Rats weighing between 50 and 60 gram from same litters were divided into three groups. Group I received a diet containing 2 grams of protein per kilo of body weight per day. Group II, 4 grams and group III, 10 grams supplemented with a definite amount of yeast and lettuce. Rats were weighed each week and the food consumed each day. The diets which were equal in caloric value were adjusted weekly according to body weight and food consumed.

A rapid growth was found in group III. Group II showed a steady gain in weight, but the rate was much slower than that in group III. Group I lost weight slowly but steadily. At the end of the 16th week the average weights of the females of the three groups were 196, 110 and 35.8 grams and of the males 285, 111 and 49 grams respectively.

The loss of weight in group I is undoubtedly due in part to the deficiency

of cystine in the diet. However, it is singular that our rats on diet II showed a steady gain, although the diet also contained less than 8 per cent of casein which according to the literature is the minimum amount for growth. Along with the gradual loss of body weight in group I there was a slow decline of food intake per day, however, the decrease in food consumption per gram of body weight was much less marked in this group than in the others. At the age of 20 weeks the intake per gram of body weight per day was 70, 58 and 37 mgs. respectively for the three groups, I, II and III.

In the metabolism studies all the foods including yeast and lettuce as well as urine and feces were analyzed. In spite of a gradual loss in body weight and the premature death of group I, a positive nitrogen balance was found in the majority of the rats studied. In the other two groups the Nitrogen balance was always positive with the maximum retention in group III. The average values of the Nitrogen retention of the three groups was 3.0, 24.8 and 62.1 milligrams per 24 hours per rat respectively. The corresponding values for per gram of body weight were 0.057, 0.276, and 0.378 mgm.

Rats in group I appeared to be markedly emaciated and inactive. With a few exceptions they died between the 16th and 22nd week. One of them, a male, lived as long as 181 days. On autopsy there was a complete absence of subcutaneous fat in group I, while in the other two groups an abundance of fatty tissue was found. The kidneys of the three groups appeared to be proportional to their body size. The average values for the eight kidneys of the three groups, I, II and III, were as follows: 5.8, 5.3, and 4.9 milligrams per gram of body weight while those of the left kidney were 5.3, 5.1 and 4.5.

Of the 63 rats autopsied pathological conditions of the organs were found in 15, of which 7 were from group I, 7, group II and 1, group III. Cloudy swelling of the kidney was observed in 10 rats of which 5 were from group I, 4, group II and 1, group III, which was killed after being on the diet for 256 days. For the last 137 days the diet contained from 30 to 35 per cent of protein varying according to the body weight of the rats. Two rats from group I and one from group II showed a cloudy swelling of the liver. Fatty metamorphosis of the liver was found in seven rats of which five were from diet II, and two from diet I. One of the rats from diet II showed a marked focal necrosis of the liver with bacterial emboli.

WEISNER, B. P. (EDINBURGH). On the Extraction and Separation of P-Factors from the Anterior Pituitary and Placenta and Their Effect upon the Immature and Senile Gonad.

WEISS, SOMA, LAURENCE B. ELLIS and GEORGE P. ROBB (BOSTON). Bodily Responses in Man During the Continuous Intravenous Administration of Histamine.

During recent years fundamental physiologic and pathologic significance has been attributed to the rôle of histamine in circulatory regulation. As far as man is concerned direct evidence for such function of histamine is still lacking. The effect of histamine in man is assumed from observations on animals in which the reaction of the circulation varies depending on the species used.

Observations were made on forty adults. The response of the cardio-

vascular system to the intravenous injection of histamine was instantaneous. The average minimal dose which was just sufficient to produce the earliest circulatory changes is 0.0003 mgm. per minute of a solution 1:100,000. The concentration of this minimal effective dose of histamine in the circulating blood is one to twenty billion parts. Adult individuals tolerated with marked circulatory reaction the continuous intravenous administration of 0.02 to 0.04 mgm. histamine per minute of a solution of 1:10,000. With uniform injection the observed bodily changes were practically stationary. Histamine is destroyed almost as rapidly as it enters the blood stream.

The following are the average results of some of the measurements obtained before and during the intravenous administration of an average dose of 0.02 mgm. of histamine per minute for a period of one to two hours.

MEASUREMENTS OF	BEFORE HISTAMINE	DURING HISTAMINE
Cardiac rate per minute.....	70	100
Arterial pressure, systolic, mm. Hg.....	113	116
Arterial pressure, diastolic, mm. Hg.....	71	70
Venous pressure, mm. Hg.....	6	7.5
Vital capacity, cc.....	4400	4300
Basal respiratory min. volume, liters.....	6.6	7.4
Basal respiratory quotient.....	0.83	0.77
Oxygen consumption per minute, cc.....	257	296
Calories per minute per square meter.....	42.3	53.2
Cardiac output per minute, liters.....	7.2	8.5
Stroke volume, cc.....	106	92
Mean velocity of blood flow, seconds.....	42	35
Blood volume, liter.....	5.06	4.98

Histamine under the condition described produces usually a dilation of the arterioles and capillaries of the skin and of the brain, with simultaneous marked dilatation of the venules. The dilator effect of histamine on the small veins is independent of its effect on the arterioles and it may be present without change in the arterioles and capillaries. Even in the presence of marked systemic response the blood pressure shows no appreciable drop in the majority of instances. Occasionally definite rise or fall in blood pressure is observed. The heart rate, cardiac output, velocity of blood flow, pulmonary ventilation and body metabolism are increased. The response of the heart with increased output is probably responsible for the lack of fall in the arterial pressure. Appreciable contraction of the bronchioles is not present. The total blood volume is unchanged, but the distribution of the arterial and venous blood volume is shifted so that the blood in the venous system is increased.

Epinephrin in a ratio of 1:30 antagonizes the effect of histamine on the cutaneous and cranial vessels. This epinephrin-histamine antagonism varies for different functions affected by histamine.

The bodily changes thus observed during the administration of histamine are not identical with those observed on patients in shock.

VON WENDT, GEORG (HELSINGFORS). **Observations on the Physiological Influence of Unipolar High Frequency Electric Discharges in Connection with Radium Irradiation.**

Clinical observations have indicated in certain conditions a very favor-

able therapeutic influence of certain varieties of unipolar, high frequency, high tension discharges, applied in a special manner and in combination with radium irradiation.

The essential differences of the metabolism of the mesenchyma and the parenchyma are discussed in detail in my "Theoretische Grundlagen der Stoffwechsellehre" in the "Handbuch der Biochemie." I have shown in my small publication "Immunität und Stoffwechsel" that the specialization of the activity of the parenchymal or specialized working cells must interfere in a high degree with their power of defense, since the ability for defense is always related to an ability for adaptation, which is not possible in a specialized cell. The parenchymal cells react principally quantitatively and not qualitatively.

Defense and especially all local defense is almost exclusively the function of the primary or mesenchyma cells. The parenchymal cells do not come in direct contact with the blood anywhere in the body. All processes, which are concerned with the food supply and the removal of waste products of the parenchymal cells, are transported by the aid of the primary cell, the mesenchyma of the region. Accordingly the ability of the parenchymal cells to work depends in a high degree on the activity of the primary cells. Modifications or disturbances of this activity can be accompanied by considerable changes of the function of the parenchymal cells, without the parenchymal cells themselves being primarily affected.

It is known that physical influences can raise to a certain degree the metabolism and the activity of the primary cells, *e.g.*, rise of temperature (see Wallgren's ultramicroscopical studies on living leucocytes). Since there was reason to believe that the therapeutic effect of the energies concerned had to be traced back to a special stimulation of activity of the primary cells and no facts in this matter were yet known, a research seemed highly desirable and was carried out on the following different lines:

1. The basal metabolism before and during the time of irradiation.
2. The nitrogen metabolism.
3. The purine metabolism with a purine-free diet.
4. The mineral metabolism.
5. The influence of irradiation during the period of vitamin deficiency (lack of fat soluble vitamins).
6. Ultramicroscopic observations upon living leucocytes.

Briefly we may say that the results show that with the energies studied we have powerful means of increasing the activity of the mesenchyma and consequently of their power of defense. The basal metabolism drops by degrees with continued irradiation, but the R. Q. drops rapidly after a very short time of irradiation.

The vitamin deficient animals show a rapid improvement in the xerophthalmia during a very long period and an extraordinary increase of weight and then a rapid breakdown.

An immediate reaction of certain leucocytes to the radiation can be observed, with a tendency to motion toward the radiation direction. A weak radium effect not to be seen microscopically under normal circumstances can be made very effective by high frequency electric discharges.

The research was carried out in the Zeileis Institute, Gallsbach, with the collaboration of Dr. med. Fritz G. Zeileis.

VON WENDT, GEORG (HELSINGFORS). **On the Biology of Iodine and Iodine Combinations. (Demonstration)**

The results of the last survey of goiter in Finland, together with a plan and the preventive measures already taken, were presented to the XIIth International Physiological Congress at Stockholm. Of the two suitable ways the one of the direct iodine administration was applied only in a small degree. A weak iodizing of bread was tried with different kinds of bread to a limited extent.

The indirect method in which the animal was fed a weak iodized fodder seemed more promising for a country in which the use of milk and milk products is very great.

Comparative research showed that this weak iodized mixture of mineral salts having a composition such that the main defects of the mineral combinations of the usual fodder were corrected, had exercised a favourable influence on the quantity of milk as well as on the fat content of the milk. The relation of this to the weak iodizing will not be discussed fully here. This favourable result has induced a more extensive use so that the quantity of one million kgm. of iodized nutrient mixture, which is quite considerable for Finland, will probably be exceeded this year. Continuing the research after the Stockholm congress, a very wide increase of goiter among the domestic animals, especially the pigs and horned cattle, was observed. In districts with much human goiter only few of the calves were without goiter. On one of the greatest estates for experimenting we found 72 per cent of the calves with goiter before administration of the iodized mineral salt; after a year of application to the milk-cows the number decreased to only 2 per cent. Also an immediate application of the iodized mineral salt mixture to calves with goiter had a good result.

In Sweden as well as in Finland it was found that with an increasing milk productivity, appearances of depression in the generative powers of the animals (sterility) increased rapidly. Generally this decreases completely with the application of the iodized mixture of mineral salt. Numerous experiments show that administration of mineral salt for half a year is sufficient to produce approximately normal values for conception.

The research is extended farther to indirect iodizing of the food by agricultural fertilizing. An increase of iodine was observed with apples. Fertilizing with metallic iodine solutions was seen to be especially effective.

A number of iodine combinations is examined regarding its influence in vitamin deficiency. One of these, cuprous iodide, has shown a very strong stimulating effect in disorders of assimilation through vitamin deficiency. The decrease of weight of the animals is succeeded immediately by an increase after administration of 0.1-0.2 mgm. So far as can be judged in regard to the present tests, the main activity is to be ascribed to copper—but other copper combinations have not given such a powerful and rapid response as was obtained with cuprous iodide.

WEST, E. S. (ST. LOUIS). **Demonstrations of Apparatus Embodying the West Type of Laboratory Condenser. (Demonstration)**

1. Different types of the condenser.
2. A compact pyrex distillation apparatus.
3. An improved lactic acid unit.
4. A simplified steam distillation apparatus.
5. A combination reflux and distillation apparatus.

WHELAN, MARY and NORMAN M. KEITH (ROCHESTER, MINNESOTA). **A Colorimetric Method for the Quantitative Determination of Nitrates in Biological Fluids.**

An accurate method for the determination of nitrates in blood and urine is necessary for the complete study of the nitrogen metabolism in cases in which nitrates are given as diuretics. The methods ordinarily used for water analysis were not satisfactory when applied to blood and urine. The gasometric method based on the reduction of nitrates to nitric oxide by ferrous chloride and hydrochloric acid gives accurate results, but the procedure is time consuming and requires large amounts of material. The methods of Caron and of Letts and Rae based on the development of a blue color by diphenylamine and diphenylbenzidine in the presence of nitrates have not proved satisfactory. However, the addition of sodium chloride to the diphenylbenzidine reagent so stabilized the color developed by this reagent as to permit of a satisfactory colorimetric determination of small quantities of nitrate. The technic used is as follows: The urine is diluted so that it will contain approximately 0.0005 mgm. of nitrate nitrogen for each five cubic centimeters. Blood is diluted 1:50 and protein is precipitated with neutral mercuric chloride. The tubes containing unknown and standard are packed in an ice bath. Five cubic centimeters of the reagent are then added slowly. The tubes are stirred gently to effect a mixing of solution and reagent, but care must be taken to prevent the development of excessive heat. Then 10 cc. of concentrated sulphuric acid are added in the same manner as the reagent. When the tubes are cool they are removed from the ice and allowed to stand for one and a half hours after the solutions have come to room temperature, and then read in a colorimeter. This method gives results which check the standard nitric oxide method of Schulze with an error of less than 5 per cent. Nitrates added to urine or blood can be recovered with an average error of less than 2 per cent.

WHITE, A. C. and A. J. CLARK (EDINBURGH). **Oxygen Use of Frog's Auricle.**

A previous study of the oxygen consumption of the frog's heart by the authors¹ showed that there was a resting oxygen consumption which was from 20 to 30 per cent of the oxygen consumption during moderate activity. A similar value was obtained both with the resting heart and the empty contracting heart. It also was found that when the mechanical response was abolished by various depressants (narcotics, lack of calcium, excess potassium), there remained a resting oxygen consumption of similar value.

These figures are open to the objection that the resting ventricle is inadequately oxygenated. The writers found that the isolated frog's auricle and tortoise's auricle had an oxygen consumption that could be measured in a Barcroft apparatus and that a normal respiratory exchange occurred through the external surface when the auricle was either empty or filled with fluid and suspended in oxygen. These preparations therefore were well suited for the study of resting metabolism.

We confirmed the conclusions made in our previous papers regarding the influence of variations in the diastolic volume on the oxygen consump-

¹ Clark and White. Journ. Physiol., 1928, lxxvi, 185, 203.

tion, and found that the oxygen use of the empty auricle was about 30 per cent of the oxygen use with moderate filling and 15 per cent of that with maximum filling.

Auricles paralysed with ethyl urethane (0.22 molar), lack of calcium, and excess of potassium chloride (10-20 millimolar), showed a resting metabolism of similar value. The oxygen use associated with contraction and the mechanical response were reduced in equal proportions by the agents mentioned.

WHITE, H. L. (ST. LOUIS). Observations on the Nature of Glomerular Activity.

From the equation $E. F. H. = G. C. P. - I. C. P. - C. O. P.$, where $E. F. H.$ is effective filtering head of pressure, $G. C. P.$ is glomerular capillary pressure, $I. C. P.$ is intracapsular pressure and $C. O. P.$ is colloidal osmotic pressure of the plasma, when $E. F. H.$ is greater than zero, filtration will presumably occur. This was found to be the case in 19 capsules in 16 specimens of *Necturus*. The glomerular capillary pressures ranged from 8.5 to 27 cm. H_2O , the intracapsular pressures from 0.1 or 0.2 to 2.8 cm. H_2O and the colloidal osmotic pressures from 6.5 to 14.2 cm. H_2O . In 9 other capsules with sluggish circulation the glomerular capillary pressure was less than the sum of the intracapsular pressure and colloidal osmotic pressure, i.e., $E. F. H.$ was less than zero. Nevertheless, these glomeruli were eliminating fluid, as shown by the fact that a minute amount of dye injected into the capsule was washed down into the tubule. From these latter observations the conclusion might be drawn that the glomerulus can eliminate fluid by a process other than filtration; an objection to this conclusion might be that the walls of those capillaries with sluggish circulation were abnormally permeable, so that the effective colloidal osmotic pressure was less than the observed. Therefore, in an additional series of experiments a small $G. C. P. - I. C. P.$ difference was obtained by raising artificially the intracapsular pressure while the glomerular capillary pressure was normal. This was accomplished by occluding the nephrostome and tubule, thus making the capsule a closed system, and inserting into the capsule a pipette containing Ringer's solution and an air bubble indicator, the pipette being connected to a leveling bulb. In 7 capsules with glomerular capillary pressures ranging from 11 to 27 cm. H_2O , fluid entered the pipette from the capsule at a time when the $E. F. H.$ was less than zero, i.e., when the sum of $I. C. P.$ and $C. O. P.$ exceeded the $G. C. P.$ The findings are interpreted as evidence of secretion by the glomerular membrane, in addition to filtration.

WHITEHEAD, R. W. and M. H. REES (DENVER). Observations on the Oxytocic Activity of Cerebro-Spinal Fluid.

In confirmation of the results reported by Hancher and Blau, it was found that cerebro-spinal fluid removed from anaesthetized dogs by puncture of the cisterna magna is usually lacking in oxytocic activity, when tested on the isolated uterus of the guinea pig. Barbital, amytal, chloralose, and ether were used as anaesthetics.

Subcutaneous or intravenous administration of the estrus-inducing hormone, prepared from placenta, in doses varying from $\frac{1}{10}$ to 5 rat units per kilo results in no increase of oxytocic activity of spinal fluid obtained from anaesthetized dogs in a period of six hours or less.

Cerebro-spinal fluid removed from unanaesthetized dogs by cisterna puncture normally shows a variable, usually slight, oxytocic activity. Fluid obtained from female dogs, immediately post partum, shows a marked oxytocic activity. The effect is still present six hours after delivery, but it has practically disappeared within 24 hours.

Subcutaneous administration of ovarian hormone, in doses of 5 rat units per kilo per day for three days, causes an increase in oxytocic activity of cerebro-spinal fluid removed by cisterna puncture from unanaesthetized dogs.

The effect of ovarian hormone in increasing the oxytocic activity of spinal fluid appears to be less marked in lactating animals than in sexually immature or pregnant female dogs.

The oxytocic activity of cerebro-spinal fluid is lost by allowing it to stand in the ice box over night.

WICKWIRE, G. C., D. J. VERDA and W. E. BURGE (URBANA, ILLINOIS).
Proof that the Stimulating Effect of Meat on Metabolism is Due in Part to the Phosphates.

It is known that the ingestion of meat increases the respiratory metabolism and that this is usually attributed to the amino acids resulting from the digestion of meat or the organic acids resulting from the deamination of the amino acids.

Fifteen hundred cc. of 0.1 per cent dextrose solution were prepared and divided into portions of 100 cc. each. Each portion was introduced into a beaker and two goldfish of approximately the same size and with a combined weight of approximately 5 grams were placed in each beaker. Air was bubbled through the solutions to insure an adequate supply of oxygen to the fish. One hundred milligrams of pulverized desiccated skeletal muscle of the dog were added to one beaker; the ash of 100 mgm. of skeletal muscle to another; the phosphate precipitated from the ash of 100 mgm. of skeletal muscle to another, and the filtrate from this phosphate precipitate was added to another beaker. Similarly desiccated plain muscle, cardiac muscle, brain tissue, pancreas, liver, spleen, and kidney, as well as the ash, phosphate precipitate and filtrate were added to another. Small portions of the solutions were removed and sugar determinations were made immediately as well as after 25 hours, at the end of the experiments, according to the method of Benedict. The results of the average of five series of experiments showed that all of these desiccated tissues, as well as the ash and the phosphate precipitate produced a marked increase in sugar utilization, and that the phosphate precipitate produced almost as much increase as the desiccated tissue. Hence the conclusion is drawn that the stimulating effect of these desiccated tissues was due almost entirely to the phosphate content.

WIERZUCHOWSKI, M., W. PIESKOW, M. LANIEWSKI and E. OWSIANY (WARSAW). **Metabolism of Dogs during Continuous Intravenous Injection of Glucose, Fructose and Galactose with Insulin.**

The three common hexoses were injected in dogs over three hours at a rate of 2 grams per kilo per hour. Respiratory exchange was measured and determinations of sugar, lactic acid and phosphorus in blood and urine were made at frequent intervals. As control physiological salt solution was injected. Comparative figures with glucose, fructose and

galactose referring to the intravenous assimilation rate, oxidation rate, specific dynamic action, and phosphorus and lactic acid metabolism without insulin and with insulin will be presented.

WIGGERS, CARL J. (CLEVELAND). **Alterations in the Left Ventricular Beat Produced by Drugs Limited to the Right Ventricle.**

It is commonly assumed that drugs and chemicals affect the ventricular beat only when brought into contact with ventricular muscle through the coronary vessels. Experiments in which ventricular fibrillation was promptly abolished and a coordinated beat was restored by successive intraventricular injections of strong KCl and CaCl_2 solutions led us to question the validity of this assumption.

To test the matter in a crucial way the following experiments were performed: Cats' hearts were perfused with Tyrode solution. The Langendorff method was employed, except that an elastic chamber was connected with the aortic cannula, thereby allowing the left ventricle to relieve itself of fluid by contracting in a natural, after-loaded manner. The inferior vena cava and pulmonary artery were ligated and a cannula was inserted *via* the superior vena cava into the right ventricle. This offered a method of introducing drugs, supplied a means of regulating the initial right ventricular pressure and was the only avenue by which fluid could escape from the right heart. By keeping the outlet away from the heart, contact with its external surface was avoided.

Since chemicals and drugs introduced into the right ventricle were unable to enter the coronary orifices or left ventricle directly and were prevented from contact with the exterior of the heart, changes in amplitude and duration of the left ventricular pressure oscillations must be attributed to absorption from the cavity of the right ventricle and transportation by way of Thebesian communications.

Results. 1. Changes in initial pressure within the right ventricle are without effect on initial pressure or pressure pulses in the left ventricle, thus obviating the possibility that changes from introduction of drugs are of mechanical origin.

2. The introduction of epinephrin, ephedrine, strophanthin, quinidine, CaCl_2 , KCl, chloral and chloroform into the cavity of the right ventricle causes stimulating or depressing effects on the left ventricle, which are similar to those of smaller doses introduced *via* the aorta and coronary system.

3. Ventricular fibrillation following faradic stimulation and unquestionably of a permanent nature can be promptly abolished by washing the right ventricle with a 5 per cent KCl solution and in some cases with Tyrode solution acidified with HCl (pH 6.6-6.8).

4. Changes in surface negativity of the left ventricle, derived by means of Garten differential electrodes are in process of being analyzed at the time this abstract is written (April).

Conclusion. Pharmacologically, the absorption of drugs from the interior of the right ventricle and their transportation to the left ventricle is demonstrated.

Physiologically, the importance of the Thebesian communications is extended; through them, substances may be absorbed and distributed to various portions of the two ventricles, not only when the coronary supply fails or is deficient, but also while a natural coronary flow continues.

WIGGERS, CARL J. (CLEVELAND). **Cinematographic Demonstration of Different Types of Ventricular Fibrillation, Different Modes of Recovery and the Nature of the Redevelopment Rhythm.**

WIGGERS, CARL J. (CLEVELAND). **Cinematographic Demonstration of the Common Forms of Clinical Arrhythmias, Produced Experimentally.**

WILLIAMS, E., F. MARSHALL and W. E. BURGE (URBANA, ILLINOIS). **Proof that the Stimulating Effect of Protein on Metabolism is Due to Urea and Amino Acids as well as the Organic Acids.**

The stimulating effect of protein on metabolism is usually attributed to the organic acids resulting from the deaminization of the absorbed amino acids. In this investigation it will be shown that the amino acids and urea as well as the organic acids stimulate metabolism or more specifically sugar metabolism.

Four hundred cc. of 0.1 per cent dextrose solution were prepared and divided into portions of 100 cc. each. Each of these portions was introduced into beakers and two goldfish of approximately the same size and with a combined weight of approximately 5 grams were introduced into each beaker. Air was bubbled through the solutions to insure an adequate supply of oxygen to the fish. To one beaker 30 mgm. of urea was added; to another 100 mgm. of a mixture of the sodium salts of acetic, propionic, valeric, caproic, glutaric and succinic acids were added; to another 70 mgm. of a mixture of the sodium salts of glycine, alanine, *l*-leucine, *dl*-valine, *l*-cystine, *d*-glutamic acid, *l*-histidine, *l*-tyrosine, *l*-tryptophane, *dl*-phenylalanine, *l*-aspartic acid, and arginine were added; and the fourth beaker to which nothing was added served for a control. Small quantities of the sugar solutions were removed from each of the beakers and sugar determinations were made according to the method of Benedict immediately and after 30 hours, at the end of the experiments. The following is the average of ten series of experiments. The control fish used 24 per cent of the sugar in 30 hours; the fish to which the urea was added used 36 per cent of the sugar; those to which the organic acids were added, 38 per cent and those to which the amino acids were added, 45 per cent. From these results it will be seen that urea increased sugar metabolism least and the amino acids most, and the increase produced by the urea and the organic acids combined was approximately the same as that produced by the amino acids alone.

WILLIAMS, R. G., B. MCGLONE and H. C. BAZETT (PHILADELPHIA). **Nerve end Organs in the Prepuce in Man. A Comparison of Histological Preparations with the Distribution of Cold and Warm Spots. (Demonstration)**

WINTERSTEIN, HANS (BRESLAU). **Mikrorespirometer zur Untersuchung des Reizungs- und Erregungsstoffwechsels. (Demonstration)**

Der Apparat ist eine Abänderung des früher beschriebenen Mikrorespirometers (Zeitschr. f. biol. Technik u. Method., 3, 246; 1913). Der zur Aufnahme des atmenden Gewebes dienende Teil besteht aus zwei durch ein kurzes Glasrohr mit einander kommunizierenden Fläschchen, von denen das eine mit dem Manometer und der Indexkapillare in Verbindung gesetzt werden kann. Durch das kurze Rohr wird der Nerv

oder andere lang gestreckte Gebilde durchgezogen und mit Vaseline abgedichtet und der Gaswechsel des in dem letztgenannten Fläschchen befindlichen Teiles in der gewöhnlichen Weise gemessen. Wird der in diesem Fläschchen befindliche Gewebsteil gereizt, so wird die Wirkung der direkten *Reizung* auf den Stoffwechsel untersucht ("Reizungsstoffwechsel"); wird der in dem anderen Fläschchen befindliche Teil gereizt, so wird die Wirkung der fortgeleiteten *Erregung* ("Erregungsstoffwechsel") bestimmt.

WOLBACH, S. B., PERCY R. HOWE and C. F. CHURCH (BOSTON). **The Pathology of Vitamin Deficiencies.**

Vitamin A deficiency. The specific effect in albino rats, guinea pigs and humans is upon epithelium. It results in the substitution of stratified keratinizing epithelium for normal epithelium in various parts of the respiratory, alimentary and genito-urinary tracts and in cornea and parocular glands. The replacement arises solely from the focal proliferation of basal cells. The growth rate of the new epithelium is rapid and formations suggestive of neoplastic properties occur in various organs of rats and guinea pigs.

Vitamin C deficiency in the guinea pig. Scorbutus is characterized by the inability of the supporting tissues to produce and maintain intercellular substances. This applies to dentin, bone matrix and collagen. The regenerative power of epidermis, endothelium, fibroblasts and osteoblasts is not affected even in complete scorbutus.

Studies of the teeth, bone and connective tissues lead us to advance the theory that the failure of cells to produce intercellular substances in scorbutus is due to the absence of an agent common to all supporting tissues which is responsible for the setting or jelling of a liquid product.

Experimental rickets in rats (vitamin D deficiency). The outstanding initial morphologic feature is the disturbance of the sequence of ossification in epiphyseal cartilages. The earliest effect is the cessation of the degenerative changes in the cartilage, normally antecedent to its penetration by blood vessels from marrow and periosteum.

The cartilage cells continue to proliferate. They enlarge, remain viable and form a barrier beyond which blood vessels proliferate. Accompanying the vascular proliferation an excess of bone matrix is formed. Concomitantly the zone of provisional calcification is not maintained and the bone matrix subsequently deposited does not calcify.

Conversely the first morphologic evidence of repair is seen in the "degeneration" of the swollen cartilage cells and their penetration by blood vessels.

WOODRUFF, ALICE MILES, C. EUGENE WOODRUFF and ERNEST W. GOODPASTURE (NASHVILLE). **Fowl-pox. II. The Nature of the Virus as Indicated by Further Morphological Data, and by Experiments with Certain Chemicals.**

Stained preparations show that the inclusion bodies of fowl-pox are made up of large numbers of minute round structures 0.25 of a micron in diameter—the so-called Borrel bodies. In the attempt to determine what relation these two morphological structures, the inclusion bodies and the Borrel bodies may have to the disease, the effect of chemicals has been ascertained first upon free inclusion bodies obtained by tryptic digestion

and second upon ground and filtered material believed to be made up chiefly of Borrel bodies. The inclusion bodies have been found still infectious after being in contact with 1 per cent phenol for four hours, while the same bodies withstand the action of 1 per cent KOH for from 24 to 96 hours. A suspension of the Borrel bodies, on the other hand, is found to have lost its infectiousness after 4 to 20 hours in 1 per cent KOH. The greater resistance of the inclusion bodies may be due to their lipoid component as well as to the marked concentration of infectious material within each body. This greater resistance further indicates that the active agent of fowl-pox is contained within the inclusions rather than superficially adsorbed upon them.

In papers published by Sanfelice a nucleoprotein is reported to have been extracted from the fowl-pox lesion, this nucleoprotein being capable of transmitting the disease. After carefully following the technic employed by Sanfelice our experiments would indicate that inclusion bodies are probably contained in the material supposed to be a pure nucleoprotein, thus accounting for the successful inoculation of material after many hours in KOH. Since our experiments further indicate that both inclusions and Borrel bodies are able to withstand the effect of 1 per cent KOH for a definite period beyond which "reactivation" with acetic acid is impossible, the virus is believed to be not a chemical agent but a living organism.

WORONZOW, D. S. (SMOLENSK). Zur Frage über das Refraktärstadium des Nerven.

Der Nervenimpuls unterliegt auf seinem Wege zum Muskel entweder nur der Wirkung der Kathode, oder nur der der Anode des Induktionsstromes. Es wurden die Grösse der Muskelzuckung und des Aktionsstromes des Muskels oder des Nerven registriert (Saitengalvanometer).

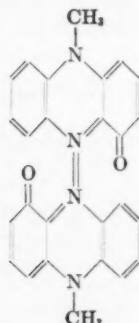
Unter diesen Bedingungen wird, wie es schon von mir (Pflüger's Arch., cxxi) gezeigt wurde, das Refraktärstadium bedeutend gekürzt, aber gleichzeitig mit dieser Kürzung zeigt die Kathode das zweite Refraktärstadium, das dem Ende des absoluten und dem Anfang des relativen Refraktärstadiums entspricht, das auf gewöhnliche Art bestimmt wurde. Die Elektrogramme zeigen, dass diese Abkürzung mit dem Erscheinen des zweiten Aktionsstromes im Muskel und im Nerven im Zusammenhang steht. Das zweite Refraktärstadium für die Kathode, die desto bedeutender ausgeprägt ist, je stärker der Strom, hängt entweder mit völliger Abwesenheit des zweiten Aktionsstromes sowohl im Muskel als auch im Nerven, oder mit seiner bedeutenden Schwächung zusammen. Zur Abkürzung des absoluten Refraktärstadiums durch die Kathode sind jedoch Ströme einer gewissen Optimalkraft erforderlich. Diese Abkürzung erhält man weder bei schwachen noch auch bei sehr starken Strömen. Die Anode gibt nur die Abkürzung, welche ebenfalls mit dem Erscheinen des zweiten Aktionsstromes begleitet wird, zeigt aber nicht das zweite Refraktärstadium. Die Elektrogramme jedoch zeigen, dass die Anode in bedeutendem Masse den Aktionsstrom des ersten Impulses schwächt, wenn sie auf den Anfangsteil des Prozesses der Erregung fällt.

Auf diese Weise entspricht das Refraktärstadium, das auf gewöhnliche Art bestimmt wird (die genäherten Pole), nicht der wirklichen Lage im Nerven oder Muskel, sondern wird in bedeutenden Masse durch die Eigenschaften des Reizes bestimmt. Der Nervenprozess in dem Stadium,

welches dem Ende des absoluten und dem Anfang des relativen Refraktärstadiums entspricht, zeigt eine desto geringere Erregbarkeit im Verhältnis zur Kathode des Induktionsstromes je stärker dieser Strom ist. Durch dieses Stadium und nicht durch die Verlängerung des absoluten Refraktärstadiums wird Wedenskys Hemmung bestimmt, daher muss man es das hemmende Stadium des Nervenprozesses nennen.

WREDE, FRITZ (GREIFSWAED). **Über die chemische Konstitution und die Bildungsweise einiger Bakterienfarbstoffe.**

Der *Bacillus pyocyaneus* bildet bekanntlich einen blauen Farbstoff, das Pyocyanin. Durch Aufarbeiten grosser Kulturmengen konnte genügend Material zur chemischen Untersuchung gewonnen werden (s.a. Wrede und Strack, H. S. 140, S. 1, 1924; 142, S. 103, 1925; 177, S. 177, 1928.) Das Pyocyanin hat die Formel $C_{26}H_{24}N_4O_2$. Der Abbau zeigte, dass es ein Derivat des bisher noch unbekannten α -Oxyphenazins ist. Damit ist zum ersten Male das Vorkommen eines Phenazinderivates in der Natur beobachtet. Das α -Oxyphenazin konnte synthetisiert werden, aus ihm liess sich durch Behandeln mit Methylsulfat das Pyocyanin künstlich gewinnen. Für das Pyocyanin wird folgende Formel angenommen:



Von besonderem Interesse ist die Beobachtung, dass der *Bacillus* die Synthese des Farbstoffes aus gewissen einfachen organischen Substanzen (neben anorganischen Salzen) durchzuführen vermag, während kompliziertere Stoffe, wie Zucker, ihm offenbar nicht genügen.—Weiterhin wurde der rote Farbstoff einer anderen Bakterienart untersucht. Die Substanz, die eine Farbintensität von der Grössenordnung der des Fuchsins zeigt, hat wahrscheinlich die Formel $C_{26}H_{25}N_3O$. Die Aufklärung der chemischen Konstitution wurde auf spektroskopischem Wege in Angriff genommen.

WU, HSIEN (PEPING). **A Theory of Denaturation and Coagulation of Proteins.**

The protein molecule is not to be regarded as a long straight chain but rather as a compact structure. Besides the peptide linkage by which the amino acids are joined "end to end" there are other kinds of linkages which unite different portions of the chain "laterally." These lateral linkages are very labile. The chain may be conceived to fold repeatedly at short intervals forming a three-dimensional network somewhat resembling a

crystal lattice in which the atoms are replaced by molecules of amino acids. Denaturation is the breaking up of these labile linkages. Instead of being compact the protein molecule now becomes a "diffuse" structure. The surface is altered and the interior of the molecule is exposed. This explains the decrease in solubility, increase in acid and base binding power, and the change in immunological specificity which are known to accompany denaturation.

Coagulation is the association of protein molecules involving the labile linkages. The ease with which some proteins are coagulated by purely mechanical means, such as shaking and high frequency sound waves, suggests a mechanical explanation of the phenomenon. Besides the possibility of union through the labile linkages on the surfaces, the protein molecules may become entangled as they collide.

WYMAN, LELAND C. (BOSTON). Cortical and Medullary Factors in Suprarenal Insufficiency.

A series of studies on suprarenal insufficiency in the albino rat has been approached by using normal rats, blank operated control rats, suprarenalectomized rats having autoplasmic cortical transplants but no demonstrable chromaffin tissue, and suprarenalectomized rats which exemplified all phases of suprarenal insufficiency from acute and subacute to chronic, as well as those which were normal with respect to cortical function because of the presence of gross accessory cortical tissue. The following studies have been completed; susceptibility to histamine poisoning and to anaphylactic shock, levels of the blood sugar and blood non-protein and urea nitrogen, together with some observations on temperature regulation.

The results have led to the following conclusions. Increased susceptibility to histamine poisoning and to anaphylactic shock in suprarenalectomized rats is not related to cortical insufficiency but is consequent to the lack of medullary tissue. Low blood sugar is characteristic of suprarenal insufficiency in rats and is associated with cortical insufficiency. Following double suprarenalectomy in rats the non-protein and urea nitrogen may be increased, the amount of increase tending to parallel the severity of the symptoms of cortical insufficiency. In suprarenalectomized rats the fall of body temperature upon exposure to moderate cold and the inability to recover normal temperature rapidly is correlated with the degree of cortical insufficiency which is present.

On the basis of the results of these studies and those of other investigators it is suggested that the suprarenal cortex is concerned in the steady maintenance of certain bodily conditions, while the medulla brings about rapid adjustments in the same direction under emergency conditions.

YAGLOU, C. P. and L. T. FAIRHALL (BOSTON). A Psychrometric Room and Methods for Determining Optimum Temperatures for Men at Rest and at Work. (Demonstration)

YOUNG, A. G. and F. H. L. TAYLOR (BOSTON). Biochemical Studies of Mercury Compounds.

By the use of a new electrolytic method for the determination of mercury the authors have studied:

I. The relative diffusion rates of:

Inorganic Hg Compounds	{ Potassium mercuri-tetraiodide Mercuric chloride Mercurous chloride
Organic Hg Compounds	{ Salicylate Mercurochrome
Colloidal Hg Compounds	{ Novasurol Gray oil True colloidal mercury

II. The effect of the following reagents on the rate of diffusion.

Potassium iodide
Ammonium chloride
Lactic acid
Sodium thiosulphate
Acids and bases
Calcium concentration

III. Amount of mercury per milligram of tissue deposited by constant perfusion of mercury solutions containing calcium.

IV. Distribution in the body tissues and rate of elimination of the compounds mentioned above.

YOUNG, E. GORDON (HALIFAX). **The Endocellular Enzymes of *B. Coli Communis*.**

Emulsions of *B. coli communis* have been prepared from stock cultures by growth on nutrient agar attaining concentrations of about 5×10^{12} cells per ml. These cells have been destroyed by repeated freezings and thawings over a period of several hours, cellular debris centrifuged off and the cellular extract passed through a Berkefeld candle. This liquid has been tested for its enzymic activity on certain substrates. It hydrolyses peptone at pH 7-8. It does not decompose glucose in the absence or presence of phosphate, aerobically or anaerobically.

Correlating studies of cell death by the freezing method with rate of methylene blue decolorization by the Thunberg technique have shown that dehydrogenase activity on succinic and formic acids is independent of living cell concentration but associated with cell stroma. Dehydrogenase activity on acetic and lactic acids, alcohol and glucose, is destroyed by the freezing technique. Toluene has been shown to act identically. These oxidative mechanisms have been shown to be temporarily independent of living cell concentrations.

YUEN, SING-TSONG et J. GAUTRELET (PARIS). **Le réflexe linguo-maxillaire sous l'influence de différentes substances modifiant l'excitabilité du centre respiratoire.**

Cardot et Laugier ont insisté avec Cherbuliez sur l'association fonctionnelle qui lie les centres du réflexe linguo-maxillaire et de la respiration, en particulier, sur l'influence inhibitrice de l'excitation du bout central du pneumogastrique vis à vis du R.L.M.

Nous avons recherché chez le chien chloralosé dont nous enregistrons la respiration, le seuil du R.L.M. mesuré en microcoulombs à l'aide du chariot de Dubois-Reymond, normalement et après injection intraveineuse de substances modifiant l'excitabilité du centre respiratoire directement

on par l'intermédiaire d'un nerf périphérique, le pneumogastrique notamment.

L'Adrénaline (1/10 mmg. p.k.) élève le seuil de façon prolongée (parfois 30 minutes) en moyenne de 8 microcoulombs. Si la section des pneumogastriques est sans effet, l'injection préalable d'Yohimbine supprime l'action de l'Adrénaline.

L'Aldéhyde formique (2-3 cg.p.k.) élève le seuil de façon temporaire (quelques minutes) et marquée (parfois plus de 30 mcbs.). La section des pneumogastriques retarde le phénomène et en diminue l'intensité.

L'injection d'Acétylcholine (3 mmg. p.k.), de Pilocarpine (5 mmg.p.k.), d'Yohimbine (3 mmg. p.k.), de Nigrosine après Thionine (1 cc.p.k.) élève également le seuil du R.L.M. de 5-10 microcoulombs.

Pour ces différentes substances, l'élévation du seuil est d'autant plus marquée qu'une phase apnéique a été enregistrée.

Par contre, l'Huile camphrée à 10% (2 cc.) a abaissé de quelques microcoulombs le seuil du R.L.M.; un abaissement plus marqué a été observé après injection de Caféine (1 cg.p.k.), et de lobéline (1/10 mmg. p.k.) au cours de l'hyperpnée.

En général, nous avons constaté un parallélisme net entre l'influence inhibitrice sur le respiration du réflexe oculo-respiratoire (non du R.O.C.) et l'élévation du seuil du R.L.M.

Si le réflexe oculo-respiratoire permet d'apprécier l'excitabilité du centre respiratoire, il apparaît que le réflexe linguo-maxillaire est susceptible de permettre de la mesurer.

ZAVADOVSKY, BORIS (MOSCOW). **Hormones and Plumages in Birds.**

During the last 10 years attention has been drawn by a series of writers to the peculiar morphogenetic changes which occur in the plumage of birds when fed preparations of the thyroid gland. In the present report an attempt is being made to complete our knowledge of the rôle played by thyroxine and other hormones in the morphogenesis of the feather and to settle some formal contradictions which have arisen between our data and generalisations and those of other writers.

I. Activation or depression of the pigment formation?

1. Experiments on brown leghorns and other chickens with a mixed color have shown that melanisation of the feather takes place when small doses of thyroid gland from 0.1 gram a day and over are being fed to the animals, while depigmentation phenomena are being observed beginning with 0.5 gram.

2. These melanisation phenomena seem not to be regarded as an activation of the pigment-forming processes but rather as a substitution of a more labile red pigment—phaeomelanin—by eumelanin which is more resistant against thyroxine.

II. Does thyroxine action reveal sex specificity?

3. About 30 leghorns have been fed with various doses of the thyroid gland and the character of the feather has been followed up regenerating in the denuded spots which are the most characteristic in regard to sex dimorphism, *i.e.*, on neck, chest and saddle.

4. Independently of the dose applied the regenerating male feather while showing most evident symptoms of melanisation does not however prove any character of the feminine type except for the rounding of the tips of the feathers and degradation of the lacy border of naked barbs.

5. In the leghorn females together with analogous changes in the structure and some melanisation of the feather peculiar changes have been noted in the pigmentation of the neck feather, redistribution of the black pigment which reverses its situation from a longitudinal to a transverse one.

6. In young females whose ovaries were not yet fully active and also in castrates of both sexes the melanisation of the feather follows the masculine type.

7. The above facts bring us to the conclusion that the redistribution of the pigment in the feather of leghorns is to be regarded as a specific effect of interference of antagonistic influences of the thyroid hormone on one hand and the feminine sex hormone on the other.

8. On the other hand the mere fact that the thyroid gland when fed to castrated females does not prevent the appearance of plumage of a feminine type or a sexless type excludes the idea of the thyroid hormone as a factor which determines the feminine type of the plumage.

III. Does the follicular hormone influence the sex type of the feather?

9. Up to 400 M. U. of menformone when injected daily into castrates does not produce any feminine character in the plumage which is being regenerated during the experiment. Neither does it prevent the regeneration of the feather of the castrate type in hens previously castrated.

10. This makes us conclude that it is not the folliculin which determines the character of chickens' feathers but some other ovarian hormone—it may probably be the lutein hormone.

IV. What are the limits of specificity of the thyroxine action on the chicken's plumage?

11. Single injections of doses of 1.5 mgm. and more of thyroxine produce in chickens all the symptoms specific for the fresh thyroid gland on condition that no symptom of intoxication can be noted.

12. The same action is being produced by the "open ring form" of thyroxine (Kendall) and by its acetyl derivative while the "closed form" of the acetylthyroxine produces a considerably weakened effect.

13. Diiodotyrosine and diiodotryptophane give no effect even in doses up to 600 mgm.

14. Crystalline iodine produces slight symptoms of depigmentation of the feather but does not effect any immediate symptoms of moulting.

15. When introduced *per os* thyroxine produces a very weak effect in chickens but the blood of animals treated in that way and exhibiting no symptoms of moulting and depigmentation still keeps its metamorphogenetic influence when injected into axolotls.

16. The above facts suggest that thyroxine forms a series of derivatives which represent different degrees of physiological inactivity. The chicken's plumage, in contrast to amphibians which react more actively to various iodine compounds, is to be regarded as a specific reagent in the narrow circle of the proximate derivatives of thyroxine and in this respect it approaches the stimulation of metabolism in mammals.

We may thus regard the above phenomena as a very convenient test object which may render it possible to solve the problems connected with the study of the thyroid hormone, and as far as the action of thyroxine is opposed by that of the sex hormone—the same test may serve for studying the behavior of the latter.

The report is being illustrated by diapositives and skins of experimental animals.

ZAVADOVSKY, BORIS (MOSCOW). The Frontal Lobe of the Hypophysis as the Driving Power for the Sex Glands.

On the basis of the fundamental works of Ph. Smith and B. Zondek and Aschheim a series of experiments has been carried through in order to complete and elaborate the problem of interaction of the sex glands and hypophysis in mammals and birds.

I. 1. Comparative activity of the hypophysis in different animal classes has been followed up.

2. The chicken's hypophysis when implanted in single doses under the skin of mice showed its full activity which was even greater than that of mammals (dogs).

3. The activity of the frog's hypophysis has been shown to coincide qualitatively with that of mammals and birds.

4. The hypophysis of the axolotl is considerably less active in comparison with other animals. This fact is being interpreted in connection with the rôle played by the former in metamorphosis and neotenia in amphibians.

II. 5. A method of extraction of the pituitary hormone from the urine of pregnant women has been worked out—whereby a very purified preparation was obtained.

6. A method of standardisation of the hormone has been worked out, by means of measurements of the hypertrophied vesiculae seminales of male mice and rats, whereby a masculine *mouse unit* has been established under identical conditions of injection which is equal to 2 feminine units (1 MMU = 2 FMU) and corresponding coefficients for the reaction in rats have been determined.

III. 7. The effect of the pituitary hormone on the sex glands and maturation in birds has been studied.

8. The pituitary hormone extracted from the pregnant urine when injected during 6 to 8 days into pigeons in the winter season produces clear symptoms of wakening and hypertrophy of the sex glands and also a striking increase in the size of the oviducts in females.

9. These phenomena become less evident in the spring season when the normal wakening of the sex glands takes place.

10. Some percentage of the experimental birds showed, however, a depression of their own sex glands which, when compared with parallel observations on mammals, may serve as an indicator of the two-sided influence of this powerful agent.

ZAVADOVSKY, BORIS (MOSCOW). The Importance of the Thyroid Gland for the Nervous Activity of Animals.

It is hardly to be doubted whether or not thyroid gland has a great importance for human mental activity since the relation may be illustrated by the behavior of cretins with innate or acquired hypofunction of the thyroid gland. As to other animals many writers have not succeeded in

discovering any marked changes in the mental activity of experimental animals after complete removal of the thyroid gland.

In collaboration with a group of students the author has followed up in detail the influence of hyper- as well as hypofunction of the thyroid gland on the nervous activity of animals by means of the objective methods of conditioned reflexes. The classical methods of the salivary reflex worked out by Pavlov and motor reflexes in dogs after Bechterev have been used; in chickens an original method was worked out in detail for the study of the food motor reflex.

I. 1. Hyperthyroidisation with large singular doses in chickens as well as in dogs has revealed a double phased action—degradation and removal of the conditioned reflexes in the first days after feeding with thyroid gland and increase of nervous excitability and of the conditioned indices beginning with the 3rd to the 5th day.

2. When fed with small doses of the thyroid gland daily a general increase of the conditioned indices is observed whereas all the reactions become more exact including the differentiation reaction.

3. Simultaneous study of the unconditioned salivary secretion does not allow interpreting the effect of the experiments as a mere increase of excitability of the peripheral apparatus of the salivary gland but indicates some immediate changes in the activity of the brain cortex brought about by hyperthyroidisation.

II. 4. In two dogs with fully established conditioned salivary reflexes the thyroid glands have been entirely removed and changes brought about in the conditioned reflex activity of the animals have been systematically followed up in the course of 8 or 9 months up to the death of the animals, which was caused by cachexia.

5. A sharp decrease of the reflex indices has been noted together with an elongation of the latent period and diminution in the quantity of the secreted saliva; all these changes have begun on the second month after the operation and have reached about 50 per cent of their initial value.

6. This decrease of the reflex indices is accompanied practically by no alteration in the unconditioned saliva secretion, this being in contradiction with the general idea of a decrease of the food excitability accompanying hyperthyreosis. But our observations are in agreement with parallel investigations by A. G. and P. N. Kratinoff who have observed an increase in the motor activity of the alimentary tube in thyroidectomized dogs.

7. This fact makes it absolutely certain that the activity of the brain cortex as an apparatus controlling the conditioned reflexes is being disturbed after thyroidectomy, which causes a decrease of the general excitability; this agrees with the data of Walkov and Asimoff which have been obtained under different experimental conditions.

8. In the course of the last month preceding the death of the animals the conditioned reflexes in thyroidectomized animals show some increase of their principal indices.

9. When fed with small doses of the thyroid gland these indices return to their normal value.

10. The above data make it hardly doubtful that the normal activity of the thyroid gland has a great importance in supporting the excitability of the brain cortex not only in man but in other animals as well.

ZERFAS, L. G., H. A. SHONLE, E. E. SWANSON and G. H. A. CLOWES (INDIANAPOLIS). **On Surgical Anesthesia with Sodium Isoamyl-ethyl Barbiturate (Sodium Amytal).** (Cinematograph demonstration)

1. Influence of purity of the product and pH range of the solution on depth and quality of anesthesia. Sodium amytal, like other barbituric acid derivatives, undergoes hydrolysis and ultimately decarboxylation when held in solution. A highly purified, stable anhydrous preparation of the sodium salt so adjusted that its 10 per cent solution in pure, distilled water shows a pH value between 9.5 and 9.8 by the electrometric method, gives a maximum anesthetic effect with a minimum degree of toxicity when injected slowly intravenously in dogs. If acid is added cautiously to this solution to the point at which the pH value is 9.2 to 9.3 and a slight opalescence or cloudiness is exhibited, the intravenous injection of the preparation fails to give a satisfactory surgical anesthesia and causes Cheyne-Stokes breathing and other toxic effects on the respiratory center. It is consequently most important that sodium amytal used for intravenous injection in man should be not only highly purified but also accurately adjusted as regards pH range.

2. Use of ephedrine and caffeine to counteract the effect of sodium amytal. Following sodium amytal anesthesia there is frequently a somewhat prolonged period of post-anesthetic sleep from which the dog may be aroused with difficulty. It appeared desirable before using this preparation extensively for the induction of general anesthesia in man to find some means of counteracting this effect. This was accomplished in dogs by injecting a combination of ephedrine and caffeine intramuscularly. Dogs which received such injections shortly after the completion of the operation when subsequently presented with food, sniffed the food, began to eat and exhibited other signs of consciousness, whilst control dogs which had not received the ephedrine-caffeine injections remained in a stuporous condition.

This highly purified and accurately adjusted preparation has been used successfully for human anesthesia in upwards of a thousand cases.

ZIH, A. (DEBRECEN, HUNGARY). **On the Influence of the Quality of Foodstuffs on Haematopoiesis.**

According to the present state of our knowledge the quality of the foodstuffs has no influence on the number of red blood corpuscles in the adult animal. Only the lack of vitamins B and C causes a decrease in the number of red blood corpuscles. It is interesting that even in the case of a diet deficient in iron, the anaemic condition only presents itself in the next generation.

Contrary with this general view I have shown that rabbits kept on a diet rich in vitamins, quantitatively perfectly satisfactory, develop anaemia if the green vegetables are absent from the ratio. The decrease of the number of red blood corpuscles stops altogether or indeed it starts to increase following the introduction of grass in the diet. The same is the effect of chlorophyll. It is therefore suggested that the chlorophyll of the diet has an influence upon the production of red blood corpuscles, probably through a stimulation of the bone marrow.

Since in earlier experiments it was shown that bilirubin has a great influence on the number of red blood corpuscles, namely, that very minute doses increase their number, it is possible that the chlorophyll acts in the

same way. The bilirubin which constantly arises in the body of the haemoglobin of the red blood corpuscles acts like a hormone of haematopoietic action.

ZUELZER, G. (BERLIN). Die Wirkung von Eutonen und Glucose auf das isolierte Herz.

Wir konnten zeigen, dass das von uns aus der Leber isolierte, Eutonen benannte Hormon den Tonus und damit die Reservekraft des isolierten Herzens (Herz-Lungen-Präparat) erhöht, während sich die Coronargefäße gleichzeitig erweitern. Mit Blutgasanalysen nach Van Slyke untersuchten wir den Herzgasstoffwechsel, und fanden, dass Sauerstoffverbrauch und Kohlensäureabgabe durch Eutonongaben nicht verändert wurden. Die stärkere Durchblutung bewirkte also nicht etwa eine Besserung des *Herzvolumens* auf dem Wege, dass ein Sauerstoffmangel oder eine Kohlensäureanhäufung behoben wurden. Der Wirkungsmechanismus des Eutons liegt im wesentlichen in der Erhöhung der Sauerstoffreserve durch die Coronarerweiterung und Herzvolumenverkleinerung. Vielleicht wird auch die Ausnützung des Blutzuckers erleichtert. Wir konnten jedenfalls in 20 unter 26 Fällen auch nach Glucosegaben eine Coronarerweiterung beobachten, die mit einer Tonusbesserung verbunden war. Die Glucose bewirkte jedoch in 17 von 21 Fällen im Gegensatz zum Eutonen eine Pulsveränderung im Sinne von einer Pulsverlangsamung.

ZUNZ, EDGARD et JEAN LA BARRE (BRUXELLES). Influence de l'hyperglycémie et de l'hypoglycémie des centres nerveux supérieurs sur l'insulinose.

On déclenche une hyperglycémie dans les centres nerveux supérieurs d'un chien chloralosé B, dont la tête, complètement séparée du tronc à l'exception des pneumogastriques, est irriguée par la double circulation carotido-jugulaire d'un autre chien chloralosé et décapsulé A, auquel on injecte une dose massive de glucose par voie intrasaphène. Par la méthode d'anastomose pancréatico-jugulaire on met en évidence, chez un troisième chien réactif C, chloralosé et décapsulé, l'hyperinsulinémie compensatrice due à la réaction des centres nerveux supérieurs, transmise au pancréas par l'intermédiaire des vagues.

Pour rechercher les effets de l'hypoglycémie des centres nerveux supérieurs, on opère de façon analogue, mais on prend comme réactif un chien dépancraté et en état d'hyperglycémie. La transfusion de 20 à 30 minutes de 100 à 200 cc. de sang veineux pancréatique d'un chien normal dans la jugulaire d'un chien réactif dépancraté réduit beaucoup son hyperglycémie. Au contraire, si l'on utilise comme donneur un chien hypoglycémique par injection soit sous-cutanée d'une dose massive d'insuline, soit intraveineuse de décaméthylènediguandine, la glycémie du chien diabétique n'est pas diminuée de façon appréciable. Si l'on extirpe presque entièrement le foie de l'animal A, qui irrigue la tête isolée de B, en employant un procédé qui exclut tout accroissement de l'insulinémie du donneur, on observe que le passage du sang veineux pancréatique du tronc de B, relié seulement par les pneumogastriques à sa tête, dans la jugulaire du réactif dépancraté C, a pour conséquence un accroissement graduel parfois très accusé de l'hyperglycémie de l'animal diabétique.

L'hyperglycémie, en agissant sur les centres nerveux supérieurs, déter-

mine un stimulus, transmis par la voie des pneumogastriques, d'où résulte la frénation de l'insulinosécrétion. Il existe donc une glycosensibilité encéphalique entraînant une réaction insuliniennne compensatrice.

ZWEIBAUM, J. ET A. ELKNER (VARSOVIE). Sur les structures cytoplasmiques dans les cellules cultivées in vitro.

Quand on soumet à l'action de l'ac.osmique les cultures de tissu sous-cutané de l'embryon de poulet, après 4-6 jours, l'ac.osmique est réduit par les diverses structures cytoplasmiques d'une manière différente selon le caractère du milieu de la culture. Dans le milieu liquide (Ringer + l'extrait embryonnaire) le cytoplasme se noircit d'une manière uniforme. Dans le milieu en plasma on observe un noircissement intense des grains petits ou grands, des longs filaments ou des courts battonnets dispersés dans tout cytoplasme et au pôle actif de la cellule les accumulations des grains, des blocs uniformes fortement noircis, ou rarement, les structures en formes réticulaires. Par sa position, sa forme et ses réactions les structures apparaissantes au pôle actif correspondent à l'appareil de Golgi. L'analyse détaillée de ces structures a été faite 1° par la méthode de blanchissage de structures noircies et la coloration par la méthode de Kull et 2° par la coloration vitale de cellules au rouge neutre et le vert Janus. La première méthode ne nous a montré qu'un certain nombre des mitochondries dans le cytoplasme aussi qu' au pôle actif de la cellule. La méthode de coloration vitale nous a permis de constater en ce lieu des grandes accumulations des vacuoles du rouge neutre ou une accumulation plus ou moins grande des grains du rouge neutre et des mitochondries. Les mêmes cellules ont été fixées au Champy-Kolatschew et ensuite traitées par l'ac.osmique. La fixation provoque une rétraction de la cellule et par conséquence un rapprochement et peut-être aussi une partielle fusion des grains et des vacuoles du rouge neutre. L'osmisation noircit intensément ces structures. Un dépôt de l'osmium réduit se forme à l'intérieure et à la surface de ces structures, ce qui conduit nécessairement à la formation des blocs fortement noircis au pôle actif ou bien à l'accumulation des grains de différent grandeur ou bien encore à la formation des cordons. Ces formations nous donnent l'image de l'appareil de Golgi. Les faits observés nous autorisent de conclure que l'appareil de Golgi n'est pas une structure vraie et propre de la cellule mais résulte de l'osmisation du système vacuolaire (segregation apparatus) ou bien, d'accord avec la théorie de Parat, de l'osmisation des grains ou des vacuoles du rouge neutre et des mitochondries, accumulées au pôle actif de la cellule.